Stem cell dialogue

MRC Medical Research Council

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STEM CELL DIALOGUE

This report presents the findings of a series of public workshops and stakeholder interviews on the science and issues surrounding stem cell research. The project took place during 2008 and was carried out by the British Market Research Bureau (BMRB), initiated by the Biotechnology and Biological Sciences Research Council (BBSRC) and the Medical Research Council (MRC), and funded by the Department of Innovation, University and Skills' Sciencewise programme.

About MRC
The Medical Research Council is dedicated to improving human health through excellent science. It invests on behalf of the UK taxpayer. Its work ranges from molecular level science to public health research, carried out in universities, hospitals and a network of its own units and institutes. The MRC liaises with the Health Departments, the National Health Service and industry to take account of the public's needs. The results have led to some of the most significant discoveries in medical science and benefited the health and wealth of millions of people in the UK and around the world.
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About BBSRC
The Biotechnology and Biological Sciences Research Council (BBSRC) is the UK funding agency for research in the life sciences. Sponsored by Government, BBSRC annually invests around £380 million in a wide range of research that makes a significant contribution to the quality of life for UK citizens and supports a number of important industrial stakeholders including the agriculture, food, chemical, healthcare and pharmaceutical sectors.
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About Sciencewise
Sciencewise is a Department of Innovation, Universities and Skills funded programme to bring scientists, government and the public together to explore the impact of science and technology in our lives. It helps policy makers in Government departments and agencies commission and use public dialogue to inform decision-making in emerging areas of science and technology. Its core aim is to develop the capacity of Government to carry out good dialogue, to gather and disseminate good practice, have successful two-way communications with the public and other stakeholders, and to embed the principles of good dialogue into internal Government processes.

About BMRB
The British Market Research Bureau (BMRB) is one of the leading market research agencies in the UK and a key operating company within the Millward Brown Group which, in turn, is part of Kantar, WPP's insight, information and consultancy division. BMRB is ISO9001:2000 and ISO 20252 accredited.

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Introduction

Stem cell research has transformed our understanding of developmental biology, providing the potential to advance healthcare in a number of areas - from the identification of new drug targets in the development of pharmaceuticals to the promise of regenerative medicine.

The UK has been forefront of this research assisted by a supportive regulatory climate and favourable public opinion. However, stem cell science and technologies are rapidly progressing. The sources of human stem cells, together with advances in potential therapeutic and clinical applications, forge major ethical issues and challenges for the regulatory regime. For research to flourish, it will be important to understand and be responsive to wider social aspirations and concerns for the science.

In March 2005, the UK Stem Cell Initiative (UKSCI) was established to ensure that the UK remains one of the global leaders in stem cell research. Chaired by Sir John Pattison, UKSCI produced a wide ranging report on the central role of stem cell research to innovation in the life sciences and its importance to the UK economy more widely.[1]

UKSCI's vision is for the UK to consolidate its current position of strength in stem cell research and mature, over the next decade, into one of the global leaders in stem cell therapy and technology. To achieve this vision, five thematic areas were identified for development, together with 11 recommendations. As well as highlighting the need to fund of basic science, clinical and translational research, these recommendations also included the need to extend the favourable regulatory climate to include clinical applications and to develop a sustained and co-ordinated dialogue with the public over the next decade.

This project was developed in response to the recommendations of the Pattison Report. Initiated by the Biotechnology and Biological Sciences Research Council (BBSRC) and the Medical Research Council (MRC), and supported by the Department of Innovation, University and Skills Sciencewise programme, the main aims of the project were to:

- engage the public about developments in stem cell research, in order that their views can be taken into account in policy development by Research Councils, the scientific community and policy makers;

[1] UK Stem Cell Initiative (2005). Report and Recommendations. Available at: http://www.advisorybodies.doh.gov.uk/ukscI/ukscI-reportnov05.pdf

- contribute to creating an environment across sectors and groups that will sustain dialogue on issues relating to developments in stem cell research and their clinical applications.

In addition to these overarching aims, six objectives were identified:

- identify the range of views and concerns about the science and ethics of stem cell research amongst the wider public and their societal context

- include scientists and other stakeholders and investigate their views about stem cell research and the related social and ethical issues, involving key organisations such as the UK National Stem Cell Network and the UK Stem Cell Communications Coalition

- raise public awareness about the potential opportunities, challenges and uncertainties of stem cell research

- raise awareness among the scientific community, Research Councils and policy makers about the views and concerns of the wider public relating to stem cell research, and of the importance of dialogue

- inform development of a plan for a longer-term project of public dialogue and engagement around stem cell research

To address these issues, BMRB, in partnership with Demos and the University of East Anglia, developed a deliberative process where members of the public and specialists could discuss the science, ethics and governance of stem cells. In addition a number of expert interviews were undertaken to explore themes discussed in the workshops.

An executive summary is provided next.

Executive Summary

- There was widespread though conditional support for stem cell research and therapies.

- Support was related to the sources of stem cells, the purposes of research and the clinical risks in treatments.

- There were ethical and social concerns related to both tissue-specific stem cells (TS cells) and embryonic stem cells (ES cells).

Tissue-specific stem cells

- Adult stem cells (AS cells) were the least controversial source of stem cells, having proven clinical applications.

- Concerns related to their plasticity; the difficulty of harvesting cells from certain areas of the body; and being able to culture cells *in vitro* to make them available for clinical practice on a large scale.

- There were concerns from certain scientists, and groups opposed to embryonic research, that too little focus was given to AS cell research in the UK.

- Stem cells derived from cord blood were valued as a benign method of collection. There was support for the donation and use of cord blood for public purposes. There were concerns around the storage of cord blood for private use, due to the perceived limited clinical value of the material and the potential exploitation of parents.

- Public participants supported the right of the individual to choose whether they donated their cord blood to the NHS, chose to store it privately or requested incineration. There were concerns that the collection and storage of cord blood stem cells should be adequately governed.

- Stem cells derived from foetal material were the most controversial of all the tissue-specific sources. This was due to moral concerns, how informed consent was gained and the research purposes of foetal material.

Embryonic cell research

- The plasticity and ability to culture ES cells had significant value, relative to the limitations of adult cells.

- Whilst the research value of ES cells was highly regarded, their ultimate use in clinical practice was less so.

- For certain groups, ES cell research was a tool to understand diseases rather than something that would ultimately have widespread therapeutic use in treatments.

- For others, it was a significant way forward in understanding and developing treatments for a number serious conditions such spinal cord injury, neurological and ophthalmological conditions.

- Risk involved in treatments – particularly due to the potential for tumours to arise from undifferentiated cells in therapies and for tissue rejection - was a concern across all groups.

- Despite many of the ethical issues associated with ES cells, the morality of not treating patients with serious diseases when there were tools available to gain understanding and potential therapies generally outweighed these concerns.

- There was general acceptance of using In Vitro Fertilisation (IVF) procedures to provide embryonic stem cells, as long as consent was gained and the process regulated. However, there were a significant number of participants who held a strong ethical conviction that the creation of embryos for research was wrong.

- A key issue for IVF was with regard to informed consent around the donation of human eggs and the difficulty in monitoring the ultimate use of embryonic stem cells lines. There were significant concerns around the payment of women to donate their eggs.

- Somatic cell nuclear transfer (SCNT) was seen as promising by certain scientific and clinical stakeholders, due to the success of cloning with non-human primates.

- For the public, despite initial concerns, SCNT was believed to overcome many of the issues associated with tissue rejection that accompany other

uses of other embryonic and adult stem cells. Concerns around efficiency levels in cloning were highlighted and there were anxieties that technical problems in the procedure may have an impact on the quality and safety of stem cell lines generated.

- For the public, the creation of cytoplasmic hybrids was initially the least supported means of creating embryos for research purposes. Views changed when participants learnt that the animal egg was only used as a shell for human nuclear material and such embryos were used for research purposes only. In particular, hybrids were seen to reduce the need for human eggs for research purposes.

- There was excitement, particularly from stakeholder groups, around the potential for induced pluripotent stem cells (IPS cells) to provide the functionality of ES cells, without the attendant ethical issues.

- Despite this, it was recognised that IPS cell research was in its infancy, and there were concerns around the safety of gene modification.

Research and therapies

- Whilst the UK's research standing was perceived to be good relative to Europe and on a par with the US, there was a sense that the UK was now starting to get left behind.

- Learning how to differentiate and control stem cells, as well as overcoming the immunological issues, were viewed as the most significant factors limiting the development of treatments. There were significant concerns around the potential to form cancers or develop infections through treatments.

- The need to invest in basic research was valued by the public and stressed by professionals

- Concerns were expressed about research being pushed to deliver applications too soon, either because of public expectations or commercial pressures.

- The combined insights from adult and embryonic stem cell research were seen as fundamental in developing therapies. Many respondents believed that treatments would come from being able to reprogramme adult stem cells, using embryonic stem cells as tools to understand how to do this.

- The first wave of applications was thought to use adult stem cells for treatments for conditions such as blood disorders, liver regeneration, age-related macular degeneration, and in particular understanding cancers. Certain respondents expected to see clinical trials using human embryonic stem cells starting in about 10 years time to treat stroke victims and spinal injuries.

- Whilst participants felt that stem cell research should be directed towards serious diseases, what constitutes such a disease was contested.

- The effectiveness of existing treatments was a significant factor in considering areas for research investment. For instance, certain participants questioned whether diseases such as diabetes, despite the seriousness of the condition, should be targeted through this research in the first instance.

- It was believed that diseases prevalent in the middle class western world, such as heart disease, degenerative diseases and cancers, are likely to gain the most investment.

- Individual rights and autonomy were seen to be two of the key principles underpinning the novel use of therapies. For the majority of participants, providing there was informed consent and the risks had been fully explained, patients should be able to trial experimental treatments, particularly where the existing treatment was not effective.

- Stem cell banks were generally supported, providing that effective governance and quality control procedures were in place to avoid the exploitation of donors and to prevent the spread of diseases.

- Equality of access to treatments was a further concern. In addressing this issue, targeted campaigns toward minority groups around the donation of embryos was advocated.

- Wider research uses for stem cells were highlighted. Developing tissues from stem cells to understand disease mechanisms, targets for drugs as well as toxicology screening were seen as potential beneficial uses. Although views were mixed as to whether toxicity testing would really reduce the need for animals in research.

- The use of stem cells to better understand cancers and develop new drug treatment was particularly supported, with a minority of groups arguing

that given the potential side effects of therapeutic uses of stem cells, this area of research should be prioritised.

Funding and commercialisation

- The limits to funding were a significant factor impacting upon progress in the field. There was a funding gap identified at the translation stage between research and therapies.

- There was a need to attract venture capital through NHS investment in stem cell therapies to create a 'healthcare pull'. Coordination was needed between research councils, medical research charities and private enterprise such as regenerative, biotechnology and pharmaceutical companies. A coordinated charity campaign to raise profile and funds for stem cell research was highlighted.

- The costs of treatments versus the health and economic benefits of treating degenerative diseases were debated. In general the public were supportive of increased investment in this area, though they were concerned that treatments would not be freely available for everyone.

- There were concerns that funding may divert resources from other areas of medical research investment. Moreover, there was a concern that investment may 'medicalise' societal issues such as ageing to the neglect of care and support.

- The involvement of the private sector raised new questions about both the means and ends of research. Participants expressed concern about the social purposes to which stem cell technologies were directed, particularly if governed by private rather then public interests. The values of openness, transparency and disclosure must not be lost in commercialisation.

Regulation

- The UK was viewed as relatively sophisticated in stem cell regulation compared to most European countries.

- The consultative approach to embryonic stem cell regulations in the UK, both with Parliamentarians and public engagement was supported and built trust in governance, though there were notable exceptions to this view from Church and pro life groups.

- There was a tension highlighted between the permissive legislative framework and the tight regulation in the UK acting as ‘brake on innovation’.

- However, the regulatory framework also provided the UK with a competitive advantage in this area, in terms of the development of stem cell lines with high safety and ethical standards.

- Strong regulation was needed to build public confidence in the absence of clear tangible benefits from the work. Despite this, there were concerns around transparency and whether scientists were conducting research out of the public gaze.

- The lack of a coherent international regulatory framework, both in Europe and globally, was likely to hinder commercialisation. There were also challenges in whether the procedures set up for medical devices were adequate to govern complex live cell products.

Public engagement

- Key principles of openness, transparency and engagement with the public were valued across all groups.

- Science should be responsive to public concerns. People have an ethical right to be involved in decision making, due to the fact that they have donated the material for research.

- The culture of science often made it difficult for individual researchers to voice concerns over risks, making open discussions more difficult.

- Open discussion around uncertainties in the science was fundamental for trust in their development long term. There were concerns that private investment may limit the potential for this.

Conclusion and recommendations

1. There was conditional support for funding all avenues of stem cell research. A focus on basic and translational research should be priorities. For clinical research, priority should be given to serious diseases or injuries for which the current treatments are limited.

2. Key concerns expressed during the dialogue focused on whether research using embryonic stem cells is necessary and how 'serious' disease is

defined. These issues are likely to evolve in the future, making it difficult to establish firm guidelines on stem cell uses and donor consent. Ethics committees will need to account for donor and public views as the science develops.

3. There were significant health and wealth opportunities to be gained from stem cell research. There needs to be greater investment and coordination between public (research councils and NHS) and private (pharmaceutical and venture capital) sectors to achieve this goal. There is a significant opportunity for a coordinated campaign by medical research charities to raise the resources and profile of stem cell science.

4. The involvement of the private sector raised concerns about the means and ends of research. For public trust to be maintained, therapies should reflect public rather than solely commercial interests, with a focus on serious diseases. Moreover, the need to protect and exploit intellectual property rights needs to be balanced with the need to disclose information in the public interest. Research councils and universities should account for these factors when commercialising research.

5. Whilst legislation in the UK was supported, tight regulation and the number of relevant authorities were viewed as cumbersome by a range of groups, including researchers, clinicians and the public. There needs to be coordination between regulators to ensure the seamless transition of research into routine clinical practice, which takes account of the novel aspects of cell based therapies.

6. The governance of clinical trials was viewed as risk-averse by certain research and commercial respondents. Providing there was informed consent and potential risks had been fully explained, there was public support in trialling experimental therapies with patients. The views of patients should be paramount when making decisions around the development of stem cell therapies.

7. Future dialogue should focus on the cultures and practices of research within institutions. Whilst large structured dialogue events are important, it will be fundamental that the everyday practice and discussion of science is mindful of societal views. Uncertainties in stem cell science should be communicated openly if the public debate is to avoid being dominated by hype. Substantive areas of interest include the private banking of cord blood and the potential of induced pluripotent stem (IPS) cells.

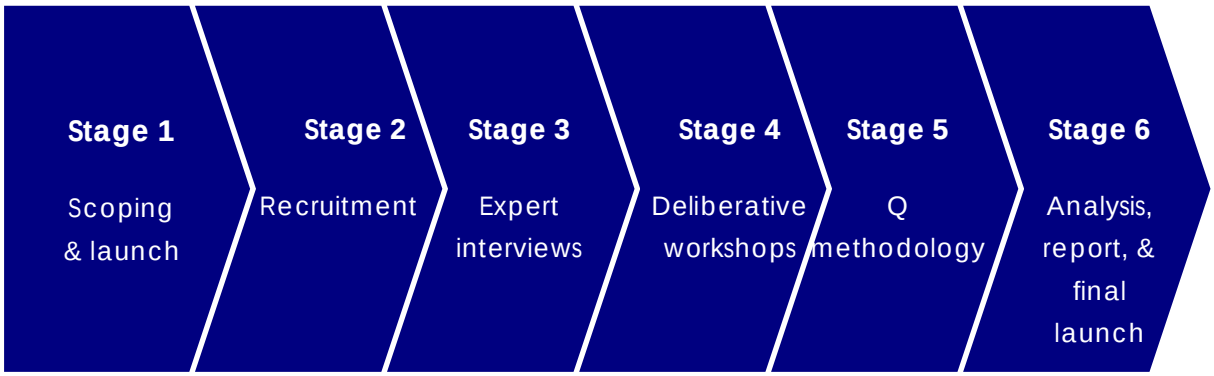
1 Methodology

The study used a variety of methodologies to engage the public and stakeholders in discussions around stem cell science and its applications. Specifically the study:

- scoped the thematic areas for the research to address;
- developed a media hook to help launch the study;
- examined the views of different stakeholders in relation to the science and ethics of stem cells;
- created a space for the public to discuss and learn about stem cells, and to engage with specialists in the field;
- analysed the data to understand the similarities and differences of the views of citizens, scientists and other stakeholders with regard to stem cell science;
- provided insight for policy makers in relation to the dialogue.

In particular, the study used a deliberative approach to engage the public. These in depth techniques are viewed as overcoming some of the limitations of top-down consultative styles, providing a forum for reflective and informed discussion between people with a range of views and values. There were six phases to the project.

Figure 1: Research phases in the stem cell study



Phase 1 – project scoping and launch: working with an Oversight Group at BBSRC and MRC, this phase detailed the focus of the study; identified stakeholders to be engaged in the process; and refined the methodology. A launch event was held during this phase and a representative survey exploring public views on stem cells undertaken.

Phase 2 – recruitment: this phase developed a structured recruitment process for stakeholders and members of the public engaged within the process. Forty-nine stakeholders were allocated to one of nine groups comprising research scientists; clinicians; church and faith groups; pro life groups; funders of research; medical research charities; regulators and government; private sector organisations; and social scientists and ethicists.

200 members of the public were recruited from across the UK, with 40 participants selected from the following areas: London, Cardiff, Newcastle, Edinburgh and Bristol. Participants were selected to reflect the local socio-economic profile of the workshop area and also to reflect the spread of UK attitudes to stem cell research.

Phase 3 – stakeholder interviews: in-depth telephone interviews were undertaken with stakeholders, each lasting approximately 45 minutes. Issues explored included the overall vision for stem cell science; the UK's position with regard to research, funding and regulation; the technical, ethical and social issues concerning TS cells; the technical, ethical and social issues concerning ES cells; and issues around clinical and other applications of the science. Interviews were audio recorded and transcribed. The interviews were used both to provide primary data for the research itself, and also to inform the content of the deliberative workshops.

Phase 4 – public dialogue: this phase involved a series of deliberative workshops engaging the public and scientists in a debate around stem cells. In each of the five UK locations, the workshops were reconvened three times. Workshop 1 introduced stem cell research and explored general aspirations and concerns for the science and clinical treatments. Workshop 2 looked in-depth at the social and ethical issues related to the sources of stem cells. Workshop 3 focused on future applications of stem cells and the wider social implications of stem cell banks, therapies and clinical trials.

Phase 5 – Q methodology: this phase involved 50 members of the public in a process to sort a series of statements made about stem cells relative to how much they agreed or disagreed with them. The results of the 'Q-sort' were then subjected to a factor analysis, to cluster individuals according to the degree of correlation between their rankings statements.

Phase 6 – analysis and report launch: this final phase involved an analysis of the workshops and interviews, through a process known as matrix mapping. First, all discussions were audio transcribed and analysed using a thematic framework. Materials were then reviewed and features identified which both characterised and explained the data. This analysis was then used to construct the report, with verbatim quotes used to illustrate the findings. A policy workshop shaped the development of the report. A final launch event brought the public, policy makers and stakeholders together to discuss the findings.

Appendix 2 provides a detailed description of the methodology. Full findings are described next.

2 Findings

2.1 Workshop 1: Visions of stem cell science

2.1.1 Introduction

The first workshop explored participants' aspirations and concerns for medical science, their understandings of stem cells and their views on a variety of stakeholder positions on the science and ethics. It specifically aimed to understand the direction, pace and visions relating to stem cell research, which inform research trajectories and investment in UK stem cell science, and which ultimately provide social context into which discussions around specific applications are given meaning.

2.1.2 Aspirations for medical science

There was widespread recognition of huge advances and developments in medical science over the years in improving mortality and morbidity rates, as well as improving quality of life. A number of specific examples were cited, from the reduction of deaths during birth and childhood and increased survival rates for cancer victims, to advances in pain relief and the effectiveness of keyhole surgery.

People discussed therapeutic applications of medical science in a wide context, from the importance of advances in basic research to social and economic impacts. Tied to this was a view of medical science as a source of national pride, allied to a desire for UK to be at the forefront of innovation and the need to move quickly to keep ahead of other countries.

They are driving commerce as well, they are driving us forward and we can't be sitting behind when other countries are going to make the money, can we?. Male, London

When asked to consider their vision of medical science in the future three main areas emerged:

Preventative medicine – there was a strong emphasis on targeting diseases at the start of their progression and preventing spread. Technologies to assist with the early detection of diseases such as cancer, heart disease and high blood pressure, particularly when coupled with lifestyle changes, were seen as valuable. Important within in these discussions was the idea of *enabling technologies* - empowering people to take control of their health.

Curative medicines – cures for diseases such as cancer were seen as the ultimate goal of medical science. Whilst a long term vision, this aspiration was

expressed in the majority of groups. In this context, the curative potential of stem cell therapies was seen to be a significant hope.

Medical Treatments – for various extant conditions, however, there was a concern that much focus in medical health was on the treatment of the symptoms of disease rather than the underlying cause – often perceived as being driven by profit motives.

I think it's within the realms of possibility to cure most things, but I do think that where we'll lead and where, when there's more money in treating something than curing it, I think that's where the advance will be made, so I do think that medicine is far more profit driven than intended to cure.
Female, Edinburgh

Participants also highlighted the need to address equity and social justice issues in the development of medical science, with treatments available for everyone, free of charge and at the point of need. In addition, eradication of disease in the developing world was cited by a number of groups as a laudable vision for science to aspire to.

2.1.3 Concerns for medical science

When participants were asked to discuss their concerns about medical science, one of the primary issues related to how commercial pressures shape and control advances. This is not to say that people thought that business involvement was bad *per se* – groups highlighted the necessity of private investment and return to develop new medical products and services. Rather, it was the diseases on which business focused that were seen as potentially problematic. In short, **medical science should be driven by social needs rather than by profit**. It was argued that social needs should not equate to government priorities for funding research – which could be changeable and politically driven – rather that informed public opinion should be taken into account.

There was a wider discussion around the pace and necessity of scientific developments. For participants, just because something was technically feasible did not mean that it should be done. Rather there was a fundamental need to ask what is socially acceptable. Importantly, scientific research needs to be done in a transparent and accountable manner, with knowledge shared amongst the scientific community.

Whilst people did not want ethics to act as a brake, it should help to steer technical developments. There were significant concerns about the potential for the unethical testing or use of medical products in parts of the world where regulation and transparency is poor.

This led to discussions around who controls science, with participants generally unaware of the nature of regulation in UK and believing that science was, to a large extent, self regulated. Many participants expressed surprise at the amount of government regulation of stem cells in subsequent discussions.

Self regulation was not viewed negatively. The overall image of scientists was positive, with researchers viewed as wanting to develop understanding of the world for public good.

Well we as a population have to have faith in the people who are doing this research on our behalf. If we don't have faith in them then there's no point is there, we have to, it's almost an institutional thing, we have to say they're there, they're there for our benefit. We just have to let them get on with it.
Male, Cardiff

However, there were concerns around disclosure of negative results, which in turn led to a wider debate on trust in science. **Overall, there was much less trust in commercial organisations than scientists working in the public arena** – though the changing nature of academic science may begin to alter this picture. More broadly, the reflection of science through the media also lessened trust – particularly around controversies such as MMR vaccinations, mobile phone masts and so on.

In addition to these issues, there were a number of specific concerns raised around the wider implications of medical science. These included a range of concerns, including prolonging life without necessarily enhancing quality of life overall; questions about how long humans should live and the burden on care and social support; and the potential to use technologies for creating 'designer babies'.

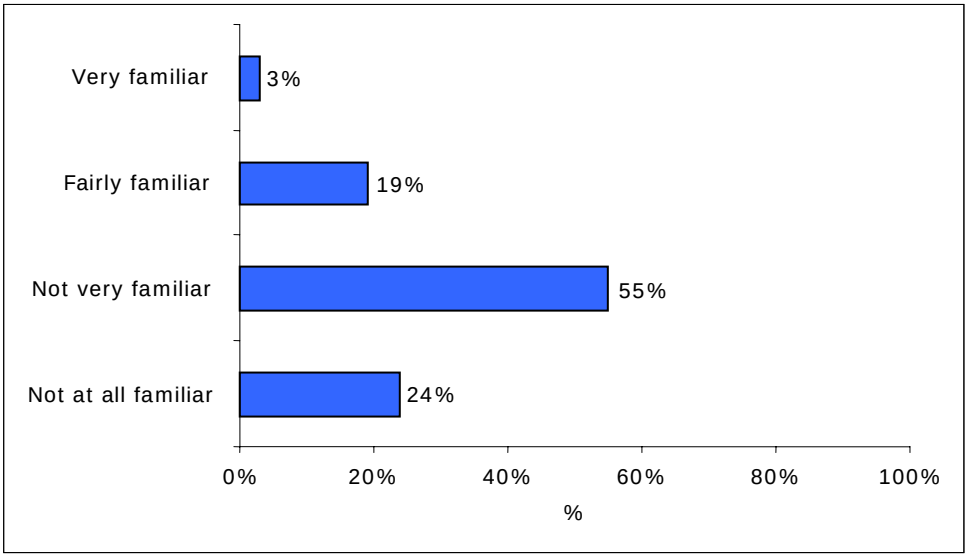
It's very much about quality of life and the philosophical question is how long are you meant to live? Is it a very good idea just to keep pushing the boundaries and living longer and longer? I think we have to sit and address ethical issues, just because we can do something doesn't necessarily mean it's a very good idea for us as human beings.

Female, Edinburgh

2.1.4 Understandings and views on stem cells

Awareness of stem cells was relatively low, with one in five claiming to be very or fairly familiar with the research and four in five either not very or not at all familiar (see figure 2).

Figure 2: How familiar are you with stem cell research?



This was borne out in the subsequent conversations which showed that while awareness of the term 'stem cells' was generally high amongst participants, detailed knowledge was patchy and inconsistent. The primary source of information was mainstream media, such as press and television, with high-profile cases such as Christopher Reeve's paralysis and subsequent stem cell campaign highlighted. In addition, certain participants had friends or family with degenerative diseases and were excited about the potential for stem cell science. There was also reasonably good knowledge around the science of stem cells – a number of participants noted that these were cell based therapies, rather than replacing whole organs:

Obviously, they are doing it to find out if they can find cures and to regenerate the cells in people's bodies that are not working. And that's the idea of the stem cells, isn't it? To replace the worn out cells in certain cases. Now that's all positive, and I have no problem with that, ethically, at all. I think that's for the good of mankind.

Male Newcastle

A number of social and ethical issues were spontaneously raised by participants, including the safety of stem cell therapies; concerns about the use of embryonic cells; the economic costs for the development of therapies; and concerns that scientists 'won't know when to stop' or may be tempted to 'play God'.

Participants were then provided with an introductory presentation on the science and ethics of stem cells. Presentations covered both adult and embryonic stem cells, in terms of their scientific scope and limitations and their current and potential clinical efficacy, as well as wider issues for the governance and regulation of stem cells in the UK and internationally. Questions raised by participants fell into four broad areas.

Table 1: Initial questions raised by participants on the science and ethics of stem cells

Technical / clinical	Safety	Ethical / social	Regulatory	Economic
How are SCs used in therapy/ do they work	What happens if you take SCs from someone who has a disease	What is the ultimate aim of stem cell research	Is there research occurring that there is no legislation for	Is there funding available aside from that from the Government
How can you control differentiation in ESCs/ how done (*in vivo* or *in vitro*)/ do you use chemicals/ when do ESCs naturally differentiate	Is the differentiation of cells safe/ how can you be sure won't change in the body	When does life begin	Can regulation keep up with advances	What is split between Government and commercial funding
Can we not just use ASCs if they are produced in the body	What happens if you use the wrong sort of stem cell in the wrong person/ concerns around heterologous treatments	Does the removal of ESCs from embryo mean it is dead	How are regulations made, and how are they enforced/ are there inspections	Why is more funding not being given
Can ASCs be changed/ is differentiation permanent	What are the potential side effects of SC therapies	What would an unethical scientist do	How do we know that embryos are not being left for longer than 14 days	Is funding limited because of moral uncertainty or uncertainty about where research will go
What can you learn from animal studies/ are they necessary		Are eggs sold/ can anyone sell	Could UK research be held back because of EU legislation	Will treatments from SCs be available via NHS or will only be available privately

Do AS cells effectiveness decrease with age		Could stem cells be used for non-medical/ bad purposes	Why is this research forbidden in Germany	
Can AS cells be harvested at death		Are stem cells needed more for research or treatment	Why is there a 14 day limit for ES cells	
How much research has moved from lab to clinic		Can stem cells be taken from aborted foetuses/ babies		

From this initial discussion, the public considered four different visions for stem cell science - from a scientific, a social science, a pro life and a commercial perspective. A debate emerged on the following issues:

The impact of advances on human dignity and autonomy

This included the dilemma of using human materials – such as treating the tissue with respect; being aware of the emotional cost of gathering material from embryos and foetuses; the instrumental use of life and creating an embryo to save another child; and the relationship between personal responsibility and healthcare advances: in particular that curative treatment may precipitate less healthy lifestyles.

Social, commercial and financial impacts

This ranged from concern that funding of stem cells meant other avenues of research would be reduced; the potential to 'medicalise' societal issues such as ageing to the neglect of care and support; the controversy of paying women to donate eggs and paying volunteers in clinical trials; the 'quick buck' mentality of the market shaping the ends of technology; and the potential to develop a two-tier health system where the wealthy will be able to buy treatments or cures unavailable to those on lower incomes, especially if too expensive for NHS.

I think with the banking of stem cells, obviously you are going to do it if you have money. What about that sort of, it's between wealthy and poor, so it's saying that if you're a millionaire you can spend thousands of pounds a year on storing your cells but if you are poor there's no chance of you having any of this because you can't afford thousands, so there's a big gap.

Female London

Whilst this latter point was a significant concern for participants, it was also argued that making treatments available could reduce much of the social care cost of degenerative diseases to NHS.

Governance

This included the expectation that Government would intervene if they thought that research was 'going too far'; that politicians do not understand the science well enough to make good decisions; and the impact of regulation on innovation and commercialisation, in terms of acting as brake on getting treatments to patients.

By rushing to commercialise it, you could be missing things and not having the right procedures and back-up in place if anything does go wrong, just rush to get this out.

Female, Edinburgh

2.1.5 Reflecting on the day

The first workshop ended with a review of the key issues from the day. These included:

- The limited public knowledge about stem cells and the need for more information and education;
- Surprise at how quickly research is moving;
- The need for limits to research;
- The need for effective regulation and international standards;
- That views had changed in relation to the ethics of research on embryos;
- That the hype around the science and its problems did not reflect the discussion participants had engaged in.

2.2 Workshop 2: Sources of stem cells

The second workshop looked in depth at the technical and ethical issues associated with different sources of stem cells. Specifically, it examined TS cells, including AS cells, those derived from foetal material and those from cord blood; and ES cells, including those derived from IVF, those from SCNT, and those from cytoplasmic hybrids; and IPS cells.

2.2.1 Tissue-specific stem cells

2.2.1.1 Adult stem cells

AS cells were seen as the least controversial source of stem cells and also as an area of research with proven clinical applications. Many participants were not familiar with the fact that bone marrow transplants and skin grafts utilised AS cells. While participants were encouraged by these breakthroughs, they questioned why advances had not been greater in this area given the 40 years since their clinical potential had been demonstrated.

In this regard, a number of technical limitations associated with AS cells were discussed including the plasticity of adult cells; the difficulty of harvesting cells from certain areas of the body, such as the brain; and the difficulties in culturing AS cells *in vitro* to make them available for clinical practice on a large scale.

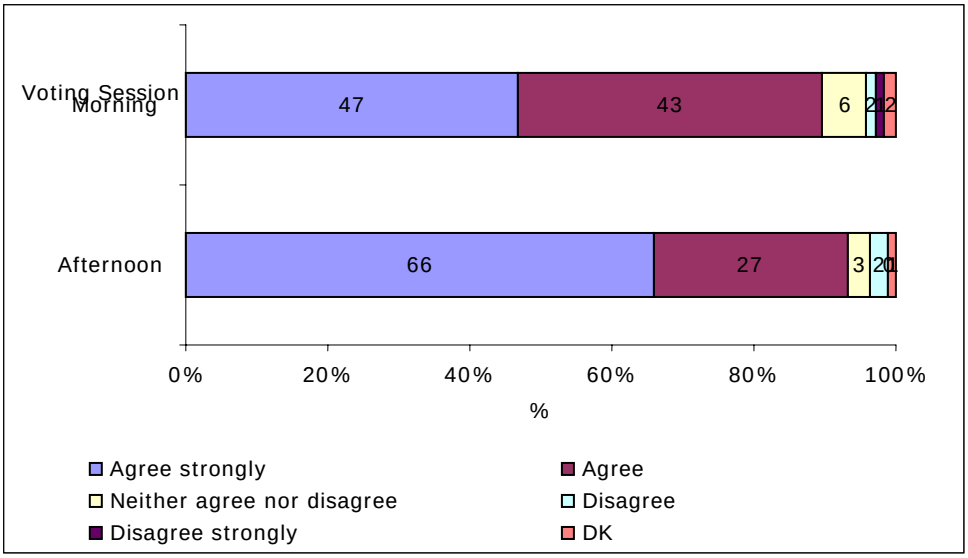
To address some of these limiting factors, there was a discussion around the potential for a national campaign to encourage the donation of AS cells, in a similar way to blood donation. However, many participants were concerned that the collection of AS cells would be a complex, painful procedure – and thus likely to limit the number of potential donors. This was particularly believed to be the case if the harvested cells were to be used for research rather than clinical purposes. Linked to this discussion, there were concerns that if there were a breakthrough in AS cell research and treatments were commercialised, it may stimulate demand for the payment for donation of adult cells, opening the potential for exploitation.

Despite these caveats, AS cells were viewed as having a proven clinical value which overcame the moral concerns of embryonic stem cells research. Treatments were viewed as progressing in terms of using patients' own AS cells for certain types of diseases. It was recognised that such treatments would be expensive - and hence potentially act as limiting factors in terms of routine clinical use - and also not suitable for all conditions. As a consequence it was thought that investment should continue in this area, particularly in terms of basic research exploring how to overcome the factors that prevent AS cells being used more widely. In this regard, a blocker to the development of this area could be the shortage of donated adult cells for research purposes.

2.2.1.2 Stem cells derived from cord blood

Stem cells derived from cord blood were viewed as a benign way to collect stem cells, overcoming the ethical issues associated with embryo and foetal-derived materials, and the invasive procedures associated with adult stem cells.

Fig 3: How much do you agree or disagree with the use of cord blood to derive stem cells?



The primary concern with regard to collection was that the safety of the mother and baby must be paramount during birth, and the collection of cord blood should not compromise this. There were related concerns that if midwives were paid by private companies to collect cord blood it would exacerbate this issue.

The donation and use of cord blood for public purposes - predominantly to treat childhood leukaemia - was supported by participants, with the material viewed as otherwise going to waste. Raising awareness of the use of donation was advocated, including campaigns that specifically sought to target Black and Minority Ethnic (BME) groups to ensure a wide range of genotypes were represented.

There were mixed views around the storage of cord blood for private use, mainly due to the perceived limited clinical value of such material to the family and the potential exploitation of parents by companies keen to hype benefits.

Notwithstanding this, participants strongly supported the right of the individual to choose whether they donated their cord blood to the NHS, chose to store it privately or requested incineration.

In this regard, there should be a more systematic process for informing people about the potential uses of cord blood during pregnancy. Background information should be given with enough time for parents to consider their options. The principle of informed consent was central to cord blood donation.

The issue of opt-outs for consent emerged spontaneously from discussion in five groups (it was not explored systematically in all workshops). Overall for these groups, providing information was given, an opt-out system was viewed as the most effective means of achieving a higher rate of donation. However, for a minority of those who discussed the issue, this was controversial and a step towards using aborted foetuses without consent.

More broadly, there were questions raised around the storage of cord blood in banks, relating to safety issues and viability of the stem cells over time, and also wider societal concerns in term of privacy and security of any information kept. The adequate governance of the collection and storage of materials was highlighted, particularly given concerns regarding Alder Hey. In this regard there were concerns about the regulation of storage, traceability of materials, screening for genetic diseases to avoid passing on illness and the potential for contamination of material. The potential for private sector use of publicly collected materials was also a concern:

I think if it is a by-product and it goes into a big bank and it helps somebody who needs it, then that's absolutely fine. But I would hate to think I gave it and somebody was making money out of it.

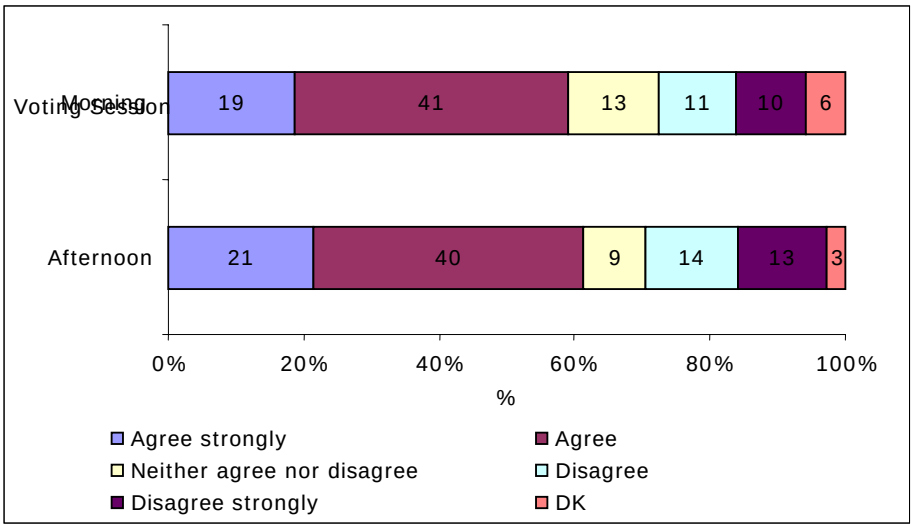
Female, Newcastle

Overall there was general unease about commercialisation of cord blood products whether for private use or to sell for research. The regulation of private cord blood banking and provision of information on the potential and limitation of therapies derived from cord blood was therefore very important.

2.2.1.3 Foetal stem cells

Stem cells derived from foetal material was the most controversial of all the tissue-specific sources considered – though 6 in 10 participants were supportive of this use.

Fig 4: How much do you agree or disagree with the use of foetal material to derive stem cells?



There were two significant concerns for participants.

The first was around the ethics of using foetal material for clinical or research purposes, with certain participants uncomfortable as to whether this was morally acceptable.

It's hard to separate my feelings about abortion from what they're being used for, so I'm finding it very difficult to answer. Because, well… as a man, it's never really going to be ultimately my choice whether it happens or not, and I understand why it does. But other than in extreme circumstances, it doesn't feel right to me.

Male, Bristol

There was also discussion as to whether there was a difference in the use material from aborted foetuses, miscarriages and stillbirths, with more permissive attitudes for non-aborted foetal material.

For the majority of participants, however, it was argued that as the material would end up being incinerated anyway, there was a duty to place it to some use. The relatively high research and clinical value of stem cells derived from foetal material compared to other tissue-specific sources was noted in this regard. As one participant stated, this was a means of ensuring *something good could come out of something bad.*

The second and greater concern for participants was not the use of material *per se* but rather the issue of informed consent. It was argued that if that if people were given more information about how foetal stem cells can be used and might be beneficial, as well as what would happen to the material, there would be a higher likelihood of donations. Clinical rather than research use of such material was preferred. The use of materials for cosmetic purposes was viewed very negatively. The difficulties of adequately governing different uses of foetal tissue were also highlighted.

There should be an ethical body that makes that decision, but for me donating stem cells from aborted foetus' and for us to say well yes you can use it for this but not for that, you know, the whole list of things that stem cells can be used for is just too complicated for me to make an informed decision you know. I should say yes you can use it or you can't and allow whatever bodies in place to ensure that you use it ethically.

Male, Cardiff

When and how consent was asked for was a key concern for participants, given the very sensitive nature of any discussion. There was a tension noted between the need to give people enough information on the potential research or clinical use of such material, set against practical concerns of not overwhelming people at a time of distress. It was generally thought that any discussion should be started prior to arrival at a hospital for a procedure. A further concern was raised as to whether consent was needed from both parents and if such a discussion could again cause distress.

The governance and regulation of this area was viewed as crucial – the need to be transparent and clear around informed consent and to develop consistent approaches across different care trusts; and to be respectful in terms of the storage of foetal stem cells.

A final set of concerns related to the potential of terminating a pregnancy to provide saviour cells for another child; or to pay others to donate such materials. The Polkinghorne guidelines were discussed in terms of the need to separate decisions relating to abortion and the subsequent use of the tissue, and by not allowing the donor to specify how her foetal tissue may or may not be used. However, as research advanced in this area, participants were concerned that there was a potential for misuse – and particularly that commercial incentives may be used in other countries with less effective governance frameworks.

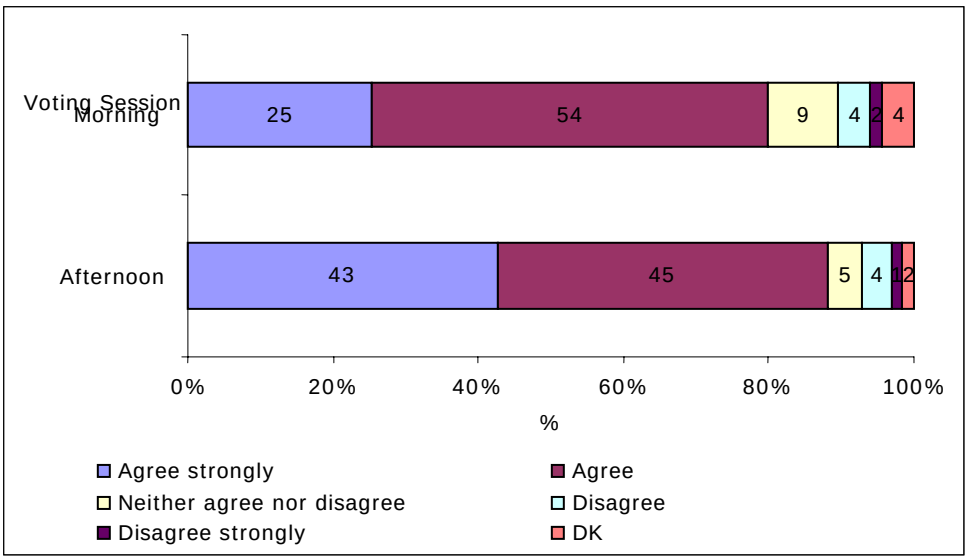
2.2.2 Embryonic Stem cells

2.2.2.1 In-vitro fertilisation

Whilst conscious of the ethical issues, generally there was acceptance of using IVF procedures to provide ES cells, as long as consent was gained and the process was well regulated. However, the process was controversial and, with the exception of foetal material, was supported less than those derived from tissue-specific cells. Discussion of the use of ES cells provoked very emotional views from certain participants.

When examining participants' votes on the issue, just over three quarters agreed with the use of ES cells derived from IVF, with one in ten opposed and the remaining participants unsure.

Figure 5: To what extent do you agree or disagree with scientists using surplus embryos from IVF treatments for research purposes?



Overall, this stance was related to the view that 'spare embryos' would otherwise be wasted. Providing the options were explained to people and consent obtained, the majority of participants were comfortable with use.

If it's a by-product, because the process of IVF, they have to create, they have to have extra eggs, that's the only way they'll get the treatment, so this is a by-product. So if, instead of destroying them they can make use in research the fine. But collecting eggs just for research I don't agree with that.

Male, Edinburgh

As figure 5 demonstrates, participant views also became increasingly permissive over the course of discussion, with 88% of participants agreeing with the use of surplus embryos for research and the proportion of those agreeing strongly increasing from 25 to 44%. There were a number of significant factors that informed participants' views in this regard, including that cells were harvested from an early stage embryo, the strict regulation of the field and the 14 day rule, all of which were discussed in detail. In particular, many people were surprised by the level of development of a blastocyst, which was seen as a ball of cells rather than as a human being.

However, there were a significant number of participants who held a strong ethical conviction that the creation of embryos for research was wrong, and the destruction of embryos as untenable, as they considered the embryos to be the beginning of human life.

Why did you create something that ought to be a human being with the intention of never actually allowing it to be? Are you morally allowed to do that?

Male, Newcastle

For these participants who held absolute rather than relative ethical standpoints, the end did not justify the means and they were unsympathetic to any work on embryonic stem cells. Participants also questioned why so many eggs were harvested during IVF procedures, and whether this was really needed to successfully conceive given the number of spare embryos created.

Beyond the ethics of the use of an embryo, one of the key issues with regard to IVF was the potential health and safety risks that women were exposed to, and in particular the issue of payment for the donation of embryos, which was viewed as very problematic.

It's one thing if a woman, or a couple, choose to donate their eggs, or their embryos, but it's another thing, I think, to incentivise…

Female, Bristol

The case of the IVF clinic in Newcastle reducing the fees in exchange for donation was viewed as controversial and, though certain participants thought it was a means of providing greater access to IVF to those who could not afford it, on balance the majority of participants believed this was potentially a means of exploiting women.

More generally, the issue of incentivising women to donate their eggs was strongly resisted due to the invasive nature of IVF, the potential for pain or discomfort to the woman, the risk of hyperstimulating the ovaries and the potential for coercion. There were significant concerns that if ES cells led to

treatments that there would be a black market in women's eggs, especially from abroad.

Beyond the ethics, one of the biggest concerns for the use of ES cells related to the risks involved in treatments – particularly due to the potential for tumours to arise from undifferentiated cells used in therapies. In addition, as stem cell lines and treatments derived through IVF were heterologous, there would be considerable issues around tissue rejection. A final concern was in regard to the fact that it was the less viable embryos in IVF that were used for research and clinical practice. Participants were concerned as to whether potential problems could manifest themselves in stem cell lines.

Finally, while the donation of 'spare embryos' from IVF was supported, the creation of embryos through this processes specifically for research was more controversial.

About foetuses being created through IVF methods purely for research and that – was the first time I had a really strong reaction to what we'd been listening to, and I mean, it was like – no way! That would really make me think. And that was the first time I'd had a really strong reaction.

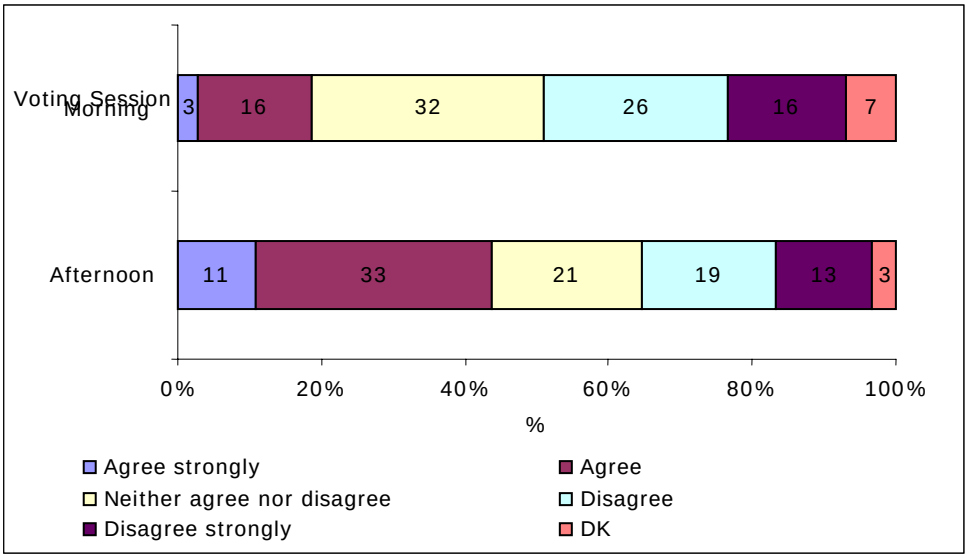
Male, Bristol

Overall, 26% of participants disagreed with the deliberate creation of embryos for research and clinical purposes – up from 15% at the start of the day. There was broader discussion as to whether women would donate embryos for research purposes, though again it was thought that the health and safety risks and discomfort meant that it would be unlikely outside of the context of IVF. Overall it was argued that if women wanted to donate their eggs for research purposes and there was informed consent, then such an avenue should be permitted.

2.2.2.2 Somatic Cell Nuclear Transfer

The use of cloning technologies to help develop embryos for research and ultimately treatments was also a controversial issue, though also one which had the most marked level of change in views: those supporting it rose from a fifth to just under a half over the course of debate.

Figure 6: How much do you agree or disagree of the use of cloning techniques to produce embryonic stem cells?



In part this was due to negative associations with the word cloning, but also due to the fact that SCNT was seen to overcome many of the issues associated with tissue rejection that accompany ES and AS cells. In this regard, cloning research was supported, as it may enable a greater proportion of society to be treated and would speed up wide access to treatment.

I mean if you're going to agree to use the left over embryos then what's wrong with them designing it for you? Otherwise you're going to reject it, or there's a higher chance of rejecting it.

Male, Edinburgh

However, there were a number of significant concerns highlighted. The current efficiency levels in cloning were discussed and there were anxieties that technical problems in the procedure may impact on the quality and safety of stem cell lines generated. In this regard, the use of SCNT for research rather than clinical purposes was more supported. Whilst the prospect of patient-specific therapies may be an ultimate goal for certain advocates of SC research, participants were more sceptical about the practical, ethical and technical limitations to this vision.

More broadly, the potential to improve the technology and facilitate human reproductive cloning was highlighted. While there was a general view that regulation may prohibit this happening in the UK, it did open up the prospect of it happening abroad. In this regard, there were concerns that once the knowledge was developed there would be people who would want to clone themselves, or use reproductive technologies for 'designer babies'. Finally, therapeutic cloning ultimately did not circumvent the need for human eggs, and if anything may exacerbate the demand for donation – promoting concerns outlined above in relation to IVF treatments.

Then you're using part of you and you're still using a donated egg, you're still using someone else's egg and that comes back to the problem of where are all these eggs coming from.

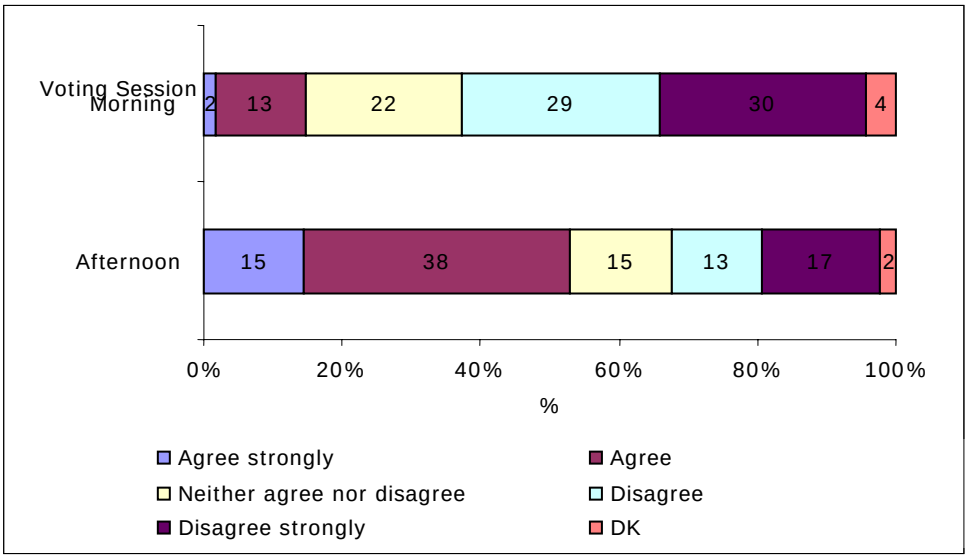
Female, Edinburgh

In considering this issue, while a significant number of participants thought the potential benefits gained from therapeutic cloning outweighed the risks, is worth noting that this was the only application that had less than half the participants either supporting or strongly supporting the technology. Overall it was seen as an avenue of research with potential benefits, but not a major priority and only one of several roads worth pursuing.

2.2.2.3 Hybrids

With 15% of participants agreeing or strongly agreeing, the creation of cytoplasmic hybrids was initially the least supported means of creating embryos for research purposes.

Figure 7: How much do you agree or disagree with creating an embryo which contains mostly human with a small amount of animal genetic material by cloning methods?



However, initial negative views of hybrids were largely overcome during the course of discussion, with levels of support rising from 15 to 53%. There were two key factors contributing to this change. First was that that the animal egg was only used as a carrier or shell for human nuclear material, that hybrids were used for research purposes only and would not be allowed, nor would be viable, to continue to maturation.

The second was that such techniques could help to overcome the need for human eggs for research purposes only, and the attendant issues of female health and the morality of egg donation – which were seen as significant drawbacks to IVF and SCNT techniques. It also meant that human ES cells could be used where they were most needed, particularly in the development of clinical grade stem cell lines. Hybrids were hence viewed as assisting with the development of SC research and helping to progress the basic science.

The discussions of this issue in the workshops coincided with the debate in the House of Commons on this issue, and many people were concerned about the 'Frankenstein' press coverage of hybrids and argued for greater public awareness and information on the issue. Certain participants likened the research as similar, in ethical terms, to xenotranplantation or the use of animals to make medical products, such as insulin from cows and pigs.

However, just under a third of participants disagreed with the creation of hybrid embryos, mainly due to the ethics of mixing human and animal materials; concerns that the procedure was not 'natural'; or that scientists would be tempted cultivate the embryos beyond the blastocyst stage. There were also latent concerns that, despite explanation to the contrary, the viable mixed embryos would be developed.

All participants agreed that regulation of this area was very important to ensure that hybrid embryos were destroyed 14 days after their creation. It was generally felt that in the UK regulation would be sufficient to oversee practice.

On balance the predominant view was that with tight regulation and providing that hybrids were used for research purposes only, the potential benefits of this research outweighed these concerns. Due to its controversial nature, research using hybrids should only be used for research into life-threatening diseases, rather than for cosmetic purposes.

2.2.2.4 Induced pluripotent stem cells

The final source of stem cells focused on the potential to induce pluripotency in adult somatic cells. It should be noted that, at the time of the workshops, creating IPS cells had only recently been achieved in adult human cells, using viral transfection systems. Discussion focused on the potential of IPS cells and health and safety issues arising.

Overall, participants felt that developments in IPS cells were remarkable – the ability to turn human skin cells into beating heart cells was astonishing and there was believed to significant potential in this area of research. Moreover, the research was less controversial, overcoming the ethical issues around the use of

embryos and the need for human eggs; and overcoming plasticity and clinical availability of AS cells.

You don't have to do all the animal hybrid thing, you don't have to go and get eggs out of babies. He's made that into an embryonic state so if he can do that we wouldn't have to sit and worry about taking it out of the cord blood at whatever stage, we don't have to take it out of the embryo within 14 or 15 days or whatever. It just seems like a turnover in history if you can do that.

Female, London

The main concerns with regard to the technique related to safety, both in terms of the potential for infection from viral transfection and the potential for tumours to arise from undifferentiated cells, in the same fashion as treatments from embryonic stem cell lines.

Overall, some of the technical detail describing advances in IPS cells was difficult for participants to grasp. For instance, the use of a virus to insert the gene factors was often associated with the use of attenuated viruses for vaccination purposes, misleading people as to the nature of potential treatments.

Finally, in the discussion of IPS cells it was also noted that innovations in the science that led to the discovery of the four gene factors was only possible due to research in embryonic stem cells and foetal material. In this regard, ES and TS cell research was viewed as complimentary.

2.2.3 Reflecting on the day

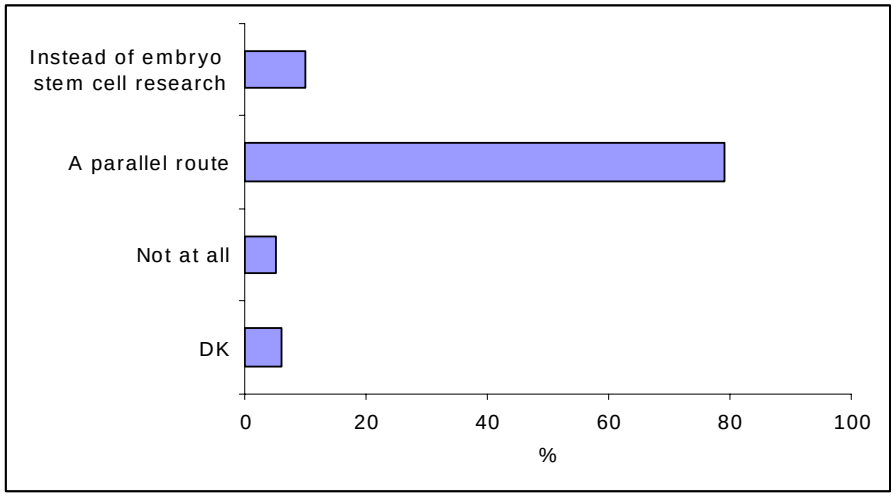
There were a number of issues that emerged over the course of the workshop. First was around the sensitivity of research in this area, and the need to be very mindful of the views of patients, those involved in the donation of materials and wider society when considering the use of stem cells.

Second was the significant amount of risk and uncertainties around treatments – and the need for a great deal of basic research to be undertaken in this area. Whilst therapies were the ultimate goal, this early work was fundamental to success in the field.

Third was that there were no single routes to development of treatments and all avenues of research should be kept open. In particular, research in one area was seen to inform another and there was a need to share knowledge to encourage learning.

In this regard, when reviewing findings over the course of the workshop, almost four in five participants felt that both research into adult and embryonic stem cells should be maintained as parallel routes.

Figure 8: Should research into adult stem cells be pursued instead of embryo stem cell research, as a parallel route, or not at all?



2.3 Workshop 3: Stem cell applications

2.3.1 Introduction

The final workshop examined the use of stem cell banks and the development of stem cell lines for different research and clinical uses. It then explored the need for informed consent and the potential treatment of different patient groups using stem cell therapies. It concluded by examining some of the non-therapeutic uses of stem cells as well as reflecting on the three workshops overall.

2.3.2 Stem cell banks

The role of stem cell banks as a repository for stem cell lines for research and therapeutic use was generally supported. There was pride that the UK was the first country to have developed a stem cell bank and there was support for expansion, on the condition that effective governance and quality control procedures were in place to avoid the exploitation of donors and prevent the spread of diseases.

There was significant concern about commercial companies 'jumping on the bandwagon' by either developing their own banks or exploiting stem cell lines for profit rather than the greater good – particularly for use in cosmetic treatments, rather than for serious diseases.

There was wider debate as to whether commercial companies *per se* should be able to access stem cell lines donated for social purposes. While certain participants held the view that embryos which have been donated for free should not be sold, the balance of opinion was that the costs involved in bringing

treatments to market and the need for private sector investment to develop treatments meant that such access was vital.

Of more importance was the need to be able to label and trace stem cell lines so that under usage can be monitored terms of consent – whilst mindful of patient confidentiality.

It was debated whether stem cell banks should have to tell donors if they discovered diseases in their cells which would affect them later in life. Individual donor views should be taken into account in this regard.

There were significant health and safety concerns around the possibility that diseases could be passed on to patients in treatments. Whilst stringent screening and safety procedures needed to be in place, on balance there was a view that it was impossible to guarantee zero risk and that recipients would have to take personal responsibility for the risk.

There was debate around the commercial exploitation of stem cell lines and discussion about whether some profits should go to donors. For concerns outlined earlier regarding incentivising donations, this was generally resisted - however there was agreement that the public investment in this area should see a return with profits coming back to academic research or directed towards NHS treatments in this area. This was related to the strong likely demand for stem cells therapies and whether such treatments would be affordable to the NHS, and free to patients at the point of need.

Building on this, there was discussion as to whether there should be free international access to stem cell lines developed in the UK. Whilst certain groups argued that the needs of the national population should come before international research access, others argued that international access would assist the progress of research for the benefit of all. Again, there was support for commercial returns to the UK for innovations developed using stem cell lines created here and used internationally.

The final concern with regard to stem cell banks was around equality of access to treatments. There were concerns that repositories may fail to include the less common tissue types, thus potentially disadvantageing BME groups. Equality of access was a key driver in the view that stem cell banks should be increased in size - to provide sufficient quantities of stem cell lines for future research and clinical practice that would benefit the diversity of the population. In addressing this issue, targeted campaigns for BME groups to encourage the donation of embryos were advocated.

I think if they are going to make so much progress with their research in this country and obviously if we want to benefit from this research I think we should make all ethnic groups aware of it because, a lot of my Bengali friends don't have

a clue about stem cells…. you should target the minority groups so they are donating as well.

Female, London

The potential of collaborating with other stem cell banks around the world was also discussed. Whilst this was to some extent supported, it was seen to precipitate issues around the safety of such lines and also the ethical procedures under which embryos in particular were donated. Whilst the governance of UK stem cell lines was viewed as trustworthy, participants were less sure about their adequacy elsewhere, particularly in emerging economies where the social and regulatory institutions were viewed as more lax.

My concern would be the ethics. If you're receiving stem cells from around the world, from other institutions you then, you circumvent or at least maybe bypass our ethical rules, we have got ethical standards and committees examining our procedures, are they the same sort of procedures and as rigorous elsewhere?

Male, Cardiff

2.3.3 The uses of stem cells in research and therapies

Building on discussion in Workshop 2, it was strongly acknowledged that it was important to undertake a considerable amount of basic research in terms of understanding and controlling the differentiation of cells *in vitro*.

However, prioritising research was difficult for participants. On the one hand, there was also a pragmatic view that spending money on research might not ultimately lead to cures or therapies. On the other, there were concerns about the potential waste of public money. In this regard, there was a view that resources should be targeted at those areas most likely to deliver.

On balance, it was argued that until the potential of stem cells are fully understood, priorities cannot easily be drawn; therefore all options should be kept open. However, future funding should be mindful of returns for investment, both in terms of clinical and financial benefits to the UK.

When considering clinical use more generally, the effectiveness of existing treatments was a significant factor in considering areas for research investment. For instance, certain participants questioned whether diseases such as diabetes, despite the seriousness of the condition, should be targeted through this research in the first instance.

It seems wasteful to spend money on that sort of research on diabetes and things like that, when an expert has actually physically told us that they have got a 60 year lifespan after treatment starts.

Male, Bristol

As such, there was generally a focus on conditions or injuries that currently had limited treatments available and which were serious, in the sense of being life-threatening or life-limiting. Cancer in particular was mentioned as an area where people hoped progress would be made, as it was seen as affecting most people either directly or indirectly at some time in their lives.

The prioritisation of particular patient groups was also discussed, specifically whether priority should be given to conditions or diseases likely to affect old or young people. Patient quality of life was central to this. Certain degenerative diseases such as Alzheimer's were seen as a high priority in this regard, though this was tempered by the likelihood of other diseases of ageing also reducing patients' quality of life.

When diseases affecting younger people were considered, the potential for tumours or the treatments having unintended and serious consequences was highlighted, problems in gene therapy treatments were discussed in this regard.

In addition, the side effects of immunosuppressant drug treatments accompanying heterologous stem cell therapies was a significant concern, and needed to be weighed up against the severity and prognosis of the condition. For a significant proportion of participants, such decisions needed to rest with scientists and clinicians, who were better able to make clinical judgements in this regard, whilst mindful of the views and needs of patients.

Drug discovery and development was an area that was also discussed in some depth. Developing tissues from stem cells to understand disease mechanisms, targets for drugs as well as toxicology screening was highlighted as beneficial uses, though views were mixed as to whether toxicity testing would really reduce the need for animals in research. The use of stem cells to better understand cancers and develop new drug treatments was particularly supported – with a minority of groups arguing that because of the potential side effects from therapeutic uses of stem cells, this area of research should be prioritised.

Across all these discussions, a key concern related to the prospect of raising hopes about what treatments might be available in the future given the current levels of success and the large problems that need to be addressed.

A strong view across all groups was the need to focus the uses of stem cells on serious medical research. Cosmetic usage was not supported and uses of stem cells to treat conditions such as acne, baldness (including when affecting women) and dental problems through the growth of new teeth should not be a focus of research. Not withstanding this, certain participants felt that if such breakthroughs were to occur elsewhere, demand in the UK for them would be great and that such treatments should then be made available.

Finally, when considering this area overall, it was felt that £25 million - the combined research spend for stem cells from MRC and BBSRC in 2005/6 - was not a huge sum of money and was dwarfed by Californian investment of $3 billion. However, there was concern about where additional money would come from, given concerns around raising taxes or diverting funds from an already overstretched NHS. A number of groups discussed the potential for public/private partnerships to develop funds, whereas others highlighted the potential to develop an integrated fundraising campaign in the UK, working across a number of medical research charities under the umbrella of stem cells. There was concern that without proper funding and investment the UK would fall behind in SC research and technology, and the US would take over as world leaders.

2.3.4 Patients and Clinical trials

The final part of the workshop focused on patients – in particular the role of the individual in decisions affecting their health, together with the risks and research ethics governing clinical trials.

Participants viewed the role of the patient as central to health decisions in this area. Individual rights and autonomy were two of the key principles underpinning clinical trials. For the majority of participants, providing there was informed consent and the risks had been fully explained, there was a view that patients should be able to trial experimental treatments, particularly where the existing treatment was not effective. Regulators should be mindful not to be too precautionary and inhibit the availability of promising treatments for diseases.

There was a debate about the potential for hype around treatments which, together with the hopes and expectations of families, may lead to pressure for individual patients to take unproven and potentially unsafe treatments. However, there was an overall view that, for terminal or degenerative conditions in particular, the potential benefits would far outweigh these concerns, and without people taking risks there would not be a major breakthrough. It was argued that novel treatments should only be used on patient groups rather than healthy volunteers. Related to that, there was concern around paying incentives for clinical trials for experimental treatments, with the incident at Northwick Park highlighted as a significant concern in this regard. Medical tourism was also discussed, with concerns that patients' lack of awareness of the science and exploitation by firms would lead to unsafe treatments abroad that could have a negative effect on the field overall.

In terms of trials for novel stem cell therapies, there were concerns around the use of placebos or absence of any treatment for control groups – rather the best available conventional medication/therapy should be used. The use of surgical procedures as part of a placebo treatment was also viewed as unethical, particularly for treatments for neural disorders. People were particularly

concerned that control groups in such trials would have their hopes raised unnecessarily and were concerned as to whether fully informed consent was possible given patient expectations. Participants queried why new treatments and therapies could not just be given to patients to see what the effects are - as long as fully informed consent was gained.

The final issue in this area related to the full disclosure of the results and side effects in clinical trials. There were particular concerns around commercial and pharmaceutical companies in this respect – recent issues concerning the transparency around anti-depression drugs were highlighted.

The issue of liability in terms of clinical trials was less clear-cut, with participants uncertain as to how informed consent would mitigate potential claims of negligence, malpractice or the adequacy of information on risks and benefits of different treatments.

2.3.5 Reflecting on the workshops

When reflecting on the workshops overall, the following issues were raised:

- given the potential significance of this area of research, why it was not higher on the public agenda;
- more research funds should be given to the area, and the need to invest in basic research, but also clinical applications;
- research was not as advanced as people thought;
- research should also consider benefits to developing countries;
- there was a general lack of public awareness about the science and its implications;
- The need for public debate that was less sensationalist and more on the justification of research;
- there are no guarantees for the research and people were not sure that stem cells will cure people.

3 Stakeholders

In addition to the public dialogue, telephone interviews were conducted with 49 stakeholders to explore professional and interest group views in depth. The structure of the interview broadly mirrored the workshop structure, with a focus on the visions, sources and applications of stem cell research. Findings have been aggregated into one of nine stakeholder groups and are described next (for a breakdown of the sample, see Appendix 1).

3.1 Research scientists

Overall vision for the science

Overall there was optimism that there would be progress in stem cell research resulting in tangible benefits to patients. Respondents were excited about the potential for regenerative medicine and the use of stem cells to understand and improve the treatment of cancers. For certain respondents, ES cell research was viewed as a tool to understand diseases rather than as ultimately having widespread therapeutic value in itself.

More broadly, it was felt that science would play a significant role in addressing the health needs of an ageing society – such applications in particular were shaped by external drivers of such as the expectations of the public, patients and politicians. However, it was acknowledged that research in this area was still in its infancy and respondents were conscious of the importance of not raising hopes, whilst still being positive about the potential of the science.

Research, regulation and funding

There was a tension highlighted across respondents between those who felt the key priority was to further interdisciplinary research on developmental biology, particularly in relation to understanding cell differentiation and control mechanisms; and those who wished to see a focus on translational research, working with clinicians and the commercial sector to address the big public health issues in the UK and internationally.

Whilst the UK's research standing was perceived to be good relative to Europe and on a par with the US, there was a sense that the UK was now starting to get left behind. The limit to funding was viewed as a significant factor impacting upon progress in the field.

There were mixed views as to whether funding strategies in the UK were effective: certain respondents argued that there was a reasonably balanced portfolio of research in the UK; others argued that the funding allocation for basic research was losing out to 'second rate translational research'; yet others argued

that there had been too much funding of embryonic stem cell research at the expense of adult research[2]:

I think the UK is being left very badly behind in stem cell research because of its very blind promotion of one type of stem cell to the detriment of the rest. The vast majority of MRC and BBSRC are actually funding that has gone into stem cells, it's gone into embryonics in the last 5 years. ES cells are useful as a tool rather than for therapies so one has to ask you know, really why is MRC paying for this.

Research scientist stakeholder

There was greater consensus on the need for private sector investment, particularly in terms of the need to attract venture capital through collaborations between research funders, regenerative medicine, biotechnology and pharmaceutical companies. The lack of investment from the NHS was viewed as short-sighted, focusing on near term costs rather than long term economic benefits:

What we have got is we have the technology push - we have got a lot of good scientists in the UK… The big problem is with lack of pull by our own leading healthcare provider in the UK, totally unlike the US where the healthcare providers would be eager to get into the space.

Research scientist stakeholder

In terms of the legislative framework, whilst it was generally viewed as positive in principle, there were concerns that it was 'repetitious' and 'painfully bureaucratic' in practice. Licensing applications were highlighted as particularly cumbersome. The proliferation of different bodies and laws covering different areas of stem cells science was also seen as complicated – a matter likely to get worse in the move into therapies. Notwithstanding this, the value of regulation was noted as helping to add to the UK's leading position - in ES cell research in particular.

More broadly, it was acknowledged that science should be responsive to public concerns, and that people have an ethical right to be involved in decision making because they have donated tissues. There were mixed views as to whether such engagement should be through patient groups or by taking into account the views of laypeople more generally.

Embryonic stem cells

Much of the current value of embryo research was viewed in relation to better understanding developmental biology. The ability to grow tissue *in vitro* was also

[2] This is not borne out by actual research spend, which is broadly proportionate across the two areas.

seen as very useful in understanding cancers and assisting the development of new drugs. While the use of ES cells for therapeutic purposes was viewed as some way off – and particularly limited through immunological responses – it was viewed as a way forward in understanding and developing treatments for a number of serious conditions, such as spinal cord injury, and neurological and ophthalmological conditions. Certain scientists questioned whether ES cells would be used in treatment, or whether developments in IPS cells would ultimately lead to the ability to manipulate cells *in situ*.

While IPS cells were considered an exciting and significant advance, there were concerns around the safety of gene modification and, more broadly, the potential for this area of research to be hyped. IPS cell research was viewed as in its infancy, and whilst warranting investment, it should not be carried out to the detriment of other research in this area.

Other areas of embryonic research such as SCNT were regarded as very promising due to the recent proof of concept work in non-human primates. Hybrids, whilst not viewed as a major area for investment, was viewed as an avenue to explore and keep open as a research tool.

In terms of ethics, reflecting on the issue personally, scientists did not have moral concerns around the use of embryonic stem cells for research: the blastocyst was viewed as a cluster of cells - indeed certain respondents saw the use of the term embryo as emotive and misleading for the public. Critical was the issue of implantation – it was only at that point where ethics came into play. For certain respondents, as long as embryos were kept *in vitro* they were no different than other human tissues. A bigger concern was the disposal of embryos that could be used for research purposes.

The issue of the limits to research was discussed. For the majority of respondents, it was argued that while there should be limits to research conducted, these have to be weighed against the potential for treatment of serious diseases.

Tissue-specific stem cells

There was seen to be the potential for advances in clinical applications from adult stem cells, particularly in understanding cancers, and in blood, skin and eye disorders. Given recent advances, it was questioned by certain respondents why there was not greater funding of this area. Notwithstanding this, the major limitation of AS cells was the inability to culture them for general clinical and research use:

Apart from the skin, we cannot grow them ex vivo at all. It's astonishing after, you know, 50 years of research and you can purify the amount of stem cells but you can't do anything with it ex vivo and, you know…. if would become possible, it would be a huge break through. It's not clear why we can't.

Research scientist stakeholder

The major advantage of AS cell research was that it was seen as ethically non-contentious and the only area to date with proven clinical value. In particular, the potential to manipulate adult cells *in situ* via the use of pharmaceuticals was seen as a private sector investment opportunity for adult cells relative to embryonic research.

Being able to pharmacologically manipulate adult stem cells in a damaged or diseased organ will happen and that's something that the pharmaceutical industry, which obviously is the one that can theoretically place large amounts of money into this, will be able to get their teeth into and will drive. I mean their problem with a lot of the stem cell biology, the sort of embryonic stem cell biology is how they can actually invest their money and how they can see a product and a profit at the end of it, but they can do pharmacology and they can manipulate adult stem cells in the brain or the heart or whatever, with a proper scientific basis of course in a time frame that, you know, they can to grips with.

Research scientist stakeholder

On balance across all research it was argued that it was not possible to know which source of stem cells was likely to be the best way forward and overall there needed to be a pragmatic approach to funding.

Therapies

It was generally thought that progress in this area would be incremental, with laboratories working on differentiation paths which may facilitate the way for regenerative medicine. It was thought likely that there would be compounds developed that could make major breakthroughs in the control of cell differentiation.

Though, overall, respondents were keen not to try and predict the nature of future therapies, for embryonic stem cells it was estimated that a major breakthrough in regenerative therapies was possible in the next decade or so, for a range of degenerative diseases. The issue of tissue rejection was substantial, however, though it was viewed as possible to overcome this through developments in IPS cell research as a route to autologous treatments.

Whether embryo or IPS or whatever, I think the major early targets are Parkinson's disease, Type 1 diabetes and perhaps heart disease and then, you

know, further up the route, I think there are things like Multiple Sclerosis, joint and bone disorders like rheumatoid arthritis, liver replacement strategies, retinal disorders like macular degeneration, Multiple Sclerosis, spinal cord damage, I think there is a very long term prospect, I don't see that happening very quickly and then I think people will get very imaginative with, with turning cells into tissues and in more three-dimensional structures like heart valves and things like that.

Research scientist stakeholder

Adult cell research offered hope in terms of treatments for the liver, the kidney, the eye, cardiac research and diabetes. It was also seen as offering great insight into the understanding of cancers:

Adult stem cell biology has been around a long time, there's practical applications of it and the obvious one that we all say is bone marrow transplantations and so stem cell plantation therapy. A couple of other examples that everybody quotes is skin grafts which can be a stem-based therapy and corneal grafts, so there are things going on that are stem cell based. There will be, very soon, many more therapies that are in some way directly related to applying or understanding adult cell biology, whether it's like I alluded to earlier about cancer therapy, I mean that's an adult stem cell biology issue. Lots of new targeting therapies, specific drugs that get at cancer stem cells will be coming out I'm sure in the not too distant future.

Research scientist stakeholder

Overall, it was acknowledged that there was no such thing as a zero risk treatment, and therapeutic developments will also depend on understanding how to prevent and deal with side effects by elucidating the mechanisms of how these cells proliferate.

3.2 Clinicians

Overall vision for the science

Whilst clinical researchers generally saw stem cell science delivering medical benefits, there was still much basic work to be done before its full potential could be realised. Certain respondents speculated that in 20 years' time many diseases will be treated at the cell level, rather than by drugs. Others observed that current research trajectories, although their outcomes were still uncertain, pointed to a future in which genetic medicine would play a major role.

Drivers of stem cell research included the rise of degenerative diseases, the shortage of organs for transplant, the obesity epidemic and associated rise in diabetes, and current concerns about the liver damage caused by high levels of

alcohol consumption. It was also acknowledged that societal expectations influence the way in which science is conducted.

Research, regulation and funding

British stem cell science was seen as being of a high standard and, for the level of investment received, very productive. The research culture was viewed as robust, open and continuing to attract good people. However, there was a general view that the level of funding was insufficient and did not match the amounts being invested in several other countries, notably the USA and Japan but also countries such as Korea and China. As a consequence the USA and Japan, although not that far ahead of the UK in terms of the basic science, operate on a different scale. One clinician expressed concern about political short-termism and knee jerk reactions to public opinion, arguing that research councils need to push the agenda rather than accept what is coming down from government.

There was a general view that the UK legislative framework was sound and relatively permissive. However, concern was expressed by certain clinicians that regulations involved paperwork that was excessively complex and time-consuming, notably in relation to animal research. Ethical approvals similarly involved “form after form” and questions that were seen as having no relevance for patients or for the research. This was seen as being a ‘real problem’. One respondent noted that, as a result of having less ethical restrictions on clinical trials and therapies, other countries are likely to get further with developing applications more quickly.

A call for increased funding was made by all respondents, although there were differences in views as to how money should be spent. Certain respondents argued that currently there was too much emphasis on the search for applications given the early stage of development of the field; others felt that there was insufficient funding for the development of effective translational research. There were also comments about the ‘stereotypical British problem’ of being good at basic research but then failing to develop or commercialise innovations effectively.

However, concerns were expressed about the research being pushed to deliver applications too soon, either because of public expectations or because of commercial pressures. The need to develop programme and project managers who understand technology transfer in academia was highlighted, to broker relationships and make the research happen. In this respect, the ‘right balance’ between basic and applied research was needed, to realise the promise of this new field of scientific research.

Certain respondents made the point that commercial involvement was essential because publicly funded institutions could not afford to bear the full costs of

developing and testing new applications through to regulatory approval. Nevertheless, it was also commented that businesses will tend to target and develop applications that they think will be successful soonest, so a robust portfolio of both public and private investment is needed for the field to develop.

Embryonic stem cells

All of the interviewees accepted the use of ES cells for research, as long as they had been ethically derived. However, certain respondents emphasised the moral status of the embryo and one clinician stated that he would not be happy working with human embryos and would be 'very unhappy' with growing embryos *in vitro*.

This was echoed by another clinician who was opposed to creating embryos purely to derive ES cell lines: "I don't think we should be creating life to destroy it". No objections were raised to any specific uses of ES cells, apart from one researcher who was uncomfortable with their use to produce artificial gametes. More generally, one respondent did not see the point of working on human ES cells until the groundwork has been done in rodents, and an understanding of how to control differentiation was established.

In general the use of unused IVF embryos for research was accepted. Certain respondents voiced concern that payment should be prevented to prevent the possibility of a market in embryos developing. One of them also objected to so-called 'egg sharing', where women who cannot afford IVF donate some of their eggs for research, in lieu of payment.

With regard to SCNT, there was a general feeling that with the success of primate cloning this area was very promising but it was also suggested by one clinician that there were questions to be answered in animal models before research on human ES cells.

With hybrids, whilst it was acknowledged that such procedures could meet the shortage of embryos, at the same time avoiding any pressure on women to donate, again certain respondents thought that much of the work in this area could be developed through animal models in the first instance and did not see the logic for the research using hybrids.

IPS cells were generally viewed as a 'major breakthrough', with benefits in helping to elucidate mechanisms of cell differentiation rather than necessarily potential therapeutic benefits. At a more philosophical level, one respondent observed that reprogramming cells changed radically our conception of what constituted an embryo, and presented an ethical challenge for the Church.

Tissue-specific stem cells

There were generally positive views around the potential for AS cell research. For certain respondents, there was a perception that this area has been under-explored because of the publicity on the embryonic side. Not withstanding this, it was noted that at present the only real adult SC therapeutics are based on bone marrow and blood cells and there was still some distance to go before treatments were more widely available.

Foetal tissue was also discussed by respondents. Whilst acknowledging the sensitivities of using such material for research, on balance respondents were comfortable, providing there was appropriate consent. It was noted, however, that there had been a very negative reaction to foetal stem cell research in the US which had been a big set back in terms of funding.

Finally, certain respondents expressed concerns about the development of commercial cord blood banks. In part this was because storage was costly and there were, as yet, no proven benefits; however it was also due to unequal access to the service if benefits were to be derived.

Therapies

A range of potential therapies was highlighted, informed by the professional perspective of respondents. The first wave of applications may include liver regeneration and treatments for conditions such as blood disorders and age-related macular degeneration. Looking further ahead, certain respondents expected to see clinical trials starting in about 10 years time using human embryonic stem cells to treat stroke victims and spinal injuries. All saw treatments for neurodegenerative disorders such as Parkinson's as being more difficult to achieve and therefore probably emerging in the following generation of therapies. The major scientific challenge was controlling stem cell differentiation, which required much more work on molecular developmental biology and genetic transcription factors.

Several of the respondents mentioned malignancy and patient safety as the biggest concern, together with the potential to transfer unknown diseases by transplanting cells. The big challenge here was therefore to develop robust ways of testing therapies without putting patients at risk. This necessitated moving ahead very cautiously and working first in animal models to reduce the risks to humans. Although there was confidence in the UK regulatory system to ensure that safety was prioritised, there was some concern that a disaster with a poorly regulated trial in another country could create a backlash that would have damageing consequences for the field as whole, with reference made to the example of gene therapy. Despite the acknowledged challenges, at least one

researcher thought that effective methods would be developed for testing cells for 'contamination'.

Given the risks, it was argued that if existing treatments provided a reasonable quality of life, there was no point in suggesting a new therapy if long term consequences were unknown. If, on the other hand, somebody was deteriorating rapidly, had a poor quality of life and there was nothing much else to offer them, then the balance shifts and it might be appropriate to try a novel therapy. In such cases, patients themselves could make an informed choice.

Finally, there was seen to be potential for stem cells in terms of drug development, particularly in terms of private sector investment; and oncology, in terms of providing a model to understand the development of cancers, rather than for their treatment.

3.3 Social scientists and ethicists

Overall vision for the science

Whilst respondents were 'cautiously optimistic' around the potential for stem cell sciences, they also highlighted the limits of biomedicine in improving human health and well being - seen as a 'medicalised view of the problems of society'. Rather the importance of factors such as social conditions, and the need to reduce health inequalities and to improve socio-economic circumstances were noted as playing a significant role.

There are certain types of medical interventions that are going to be important and people are working on those. I mean bio-medicine can help with respect to trying to address questions on Alzheimer's and dementia, and clearly stem cell has a role to play in that, you know. But I think [addressing the needs of an ageing population] is more to do with social aspects of caring of institutional structures that will help people to look after the ageing society. I think if we get it wrong there, it doesn't matter how much bio-medicine we throw at it. It's not going to be a technical fix; it needs to be a social fix really.

Social science and ethics stakeholder

Though much of the current value of stem cell research was viewed in terms of the understanding of developmental biology, there was seen to be potential in terms of technologies to aid drug development, disease diagnostics and disease management. Therapies were believed to be on the horizon and potential seen in terms of treating degenerative conditions such as Alzheimer's and dementia.

However, there were significant blockers that needed to be overcome to reach this potential, including: health and safety issues around controlling cell differentiation and toxicity; governance issues, in terms of developing coherent

international frameworks for scientific development; funding issues, in terms of venture capital investment, effective patenting and the protection of intellectual property; and clinical issues, in terms of the need to scale up stem cell lines for clinical applications and their utility compared to other treatments. How the science is 'plugged into' other technology platforms such as bio-informatics and nanotechnologies was also highlighted as a significant factor.

There was a general view that given the early stages of the science, multiple innovation routes in terms of the sources of stem cells should be pursued. However, developments in research had significant implications for public expenditure, the growth of private healthcare and health inequalities, and innovation strategies needed to take these into account.

Research, regulation and funding

The UK was viewed as being at the forefront of stem cell research and this brought with it opportunities for economic development. It was argued that a key strength was The UK's international leadership in the field. It was viewed as important that there was sufficient investment in basic science, as these insights helped ultimately to guide therapeutic applications - rather than investment being driven by particular stem cell areas, such as adult or embryonic.

The need for greater investment was identified to take the research 'to the next level', with respondents highlighting a funding gap at the translation stage between research and therapies. Another issue highlighted was capital expenditure and the need for appropriate infrastructure to ensure there are adequate facilities to develop clinical grade stem cell lines. There were concerns over how far research council investment in stem cell research can be sustained. A comprehensive overview of UK strengths and weaknesses was needed across key actors in the field to begin to help prioritise funding.

Whilst the legislative framework in the UK was viewed as broadly permissive, it was accompanied by very tight regulations that were viewed as frustrating for scientists.

Britain has been permissive on the legislation front, but what then happens is that the regulatory side of things gets tightened up, so in order for the law, the permissive law to operate and to be seen to be safe, all sort of checks and balances are put in on a regulatory side downstream amongst the experimental world of scientists and commissions, and they often find that very, very constraining compared to other countries.

Social science and ethics stakeholder

The consultative approach to embryonic stem cell regulations in the UK, both engaging with Parliamentarians and public was supported and seen to help build

trust in governance. The UK was viewed as relatively sophisticated in the regulation of this area compared to most European counties, and the HFEA viewed as a model. However, it was argued that the greatest test would come as we move closer to therapies - there were particular concerns around the interpretation of EU standards and regulation around tissue procurement and storage.

Governance becomes problematic in the issues to do with the MHRA and HTA implementing European legislation on tissue procurement and storage. Scientists are not that happy in the way in which the HTA is dealing with the issues like good laboratory practice, good manufacturing practice which are standards set up to, you know which they have to fit within. The significance of that is if that's not got right at this stage the ability to put therapeutics on the market will be limited.

Social science and ethics stakeholder

Embryonic Stem Cells

With regard to the science, the clinical potential of ES cells was recognised, due to their pluripotency, and the potential to develop clinical grade stem cell lines for mass treatment. The scale of endeavour, organisation and the 'connectedness' of UK embryonic research was seen to be a significant advantage.

SCNT was not viewed in itself viewed as a controversial procedure, though it was acknowledged that improvements in the efficiencies of techniques in this area would inevitably lead to human reproductive cloning.

IPS cells were noted as a significant advance in terms of the science and also in terms of redefining the debate between adult and embryonic cells. It was argued that such an advance helps to overcome much of the ethical dilemma associated with embryonic research, and would facilitate scientists' licence to practice in this area. Indeed, such a development also had significant implications for our understanding of ethics – in terms of where life begins and the rights we ascribe to entities such as embryos, versus reprogrammed somatic cells.

Due to the early stage of research in this area, respondents generally through it premature to consider how it may shape the science in the future. It was noted that there was significant opportunity for tissue engineering to solve immune response problems associated with ES cells.

When considering broader ethical issues, whilst respondents were supportive of the use of embryonic stem cell research, there were significant caveats around their use and the wider implications for society. The majority of respondents did not see the blastocyst as a moral entity. However, certain respondents felt it did have a moral status and were aware of the need to be sensitive to different

cultural interpretations of the value of a human embryo. Overall, research in this field needed to be justified and should only be undertaken for research into serious conditions.

A significant concern was the donation of human eggs. Consent was important, but the difficulty in monitoring the ultimate use of stem cells lines created through embryos was acknowledged. The majority of respondents did not support the production of embryos specifically for research purposes, and thought it inappropriate for healthy women to donate eggs. However, one respondent argued that it was specifically the intent of IVF to create a child, which gave such embryos a moral status. They noted:

We should probably find ways of producing them other than taking them out of IVF clinics, because there is too much value assigned to them there. That causes the problem.

Social science and ethics stakeholder

The use of hybrid embryos to overcome the shortage of human eggs, though contentious, was generally supported. Again, the social significance of these developments was highlighted - and there was seen to be a need to move forward with caution, given the emotive views from those concerned with interspecies entities, including the views from animal rights activists.

More broadly, certain respondents thought that growth in the trade of human tissue will inevitably lead to there being a market in embryos – particularly as treatments begin to demonstrate clinical success. Such a market was thought to have the potential to cause substantial complications for the governance of stem cell lines and international regulation.

The trade in human tissue is large and established and will continue regardless of what happens with the particular human embryo sub sector of that market. But if you create a demand for a particular component, then that demand will ricochet through the system will generate issues in particular countries like Romania as we know.

Social science and ethics stakeholder

Tissue-specific stem cells

It was acknowledged that research on AS cells was politically much less sensitive than human ES cell research and there was a strong consensus that research in this area should be developed. Whilst the clinical utility of AS cells was limited, it was seen as an area in which near-term clinical innovations were most likely to occur. As noted above, the potential to induce pluiportency in adult somatic cells was seen to begin to blur the distinctions between the two areas of research.

The key other area discussed was tissue from foetal material. Whilst, at a personal level, the majority of respondents viewed the use of material from abortions to be morally permissible if undertaken with the necessary consents, a more significant concern was the public reaction and, more broadly, the potential to encourage the instrumental use of aborted material and stimulate demand in research settings.

If abortion becomes a delivery service for the tissue industry or research that is a risk. And at this point, I would find that very problematic.

Social science and ethics stakeholder

Therapies

Whilst the range of diseases that could be treated by stem cells was thought to be very broad, it was argued that prevalent diseases in the middle class western world, such as heart disease and degenerative diseases were likely to gain the most investment. Cancers were also highlighted, though it was acknowledged that a range of scientific disciplines - including bioscience, genetics, biochemistry and immunology - will need to be brought together to address this area. There was a strong consensus that research should focus on serious debilitating or life-threatening diseases, rather than on cosmetic applications.

Reprogramming of cells for treatment was seen to offer promise and also help to overcome autoimmune responses. However, it was noted that the risks involved in therapeutic applications may be significant – including the potential to form cancers and spread infection. It was argued that risks need to be presented appropriately and taken seriously. Certain respondents noted that the culture of science often made it difficult for individual researchers to voice concerns over risks, making open discussions more difficult.

Manageing the risks involved would be complicated and included gaining sufficient control on the SC differentiation process; ensuring it is possible to replicate and reproduce cell lines through automation; and ensuring that clinicians know how to monitor the long term effects on patients. This was viewed to require government financial support and the development of ‘a new vigilance and training regime’.

Whilst these systemic issues were complicated, they were viewed as manageable. A bigger concern related to the societal implications of stem cells and how institutions address these:

I think our governance arrangements and the research ethics are fairly robust, although I do think sometimes the wider societal context or societal impact is out with those arrangements, so that debates around equality of access to health care, for example, outside of that framing of the whole clinical trials area. I think that is difficult.

Social science and ethics stakeholder

In terms of funding therapies, there was a gap noted between early stage and translational research. Given the horizon for bringing products to market, it was questioned whether there is enough incentive for venture capital to move into these areas to progress the technology to a therapeutic product.

Finally, manageing public expectation was also highlighted as impacting on therapies. As one respondent noted:

I think a big ethical figure on the landscape is the ways in which we can control the promises that are made about stem cells, in a way which doesn't lead to over-expectation. That may not sound like an ethical issue, but I think it is with respect to patient groups and charities that are keen to see these developments as quickly as possible, understandably for their own members. I think it's a matter of social governance, if you like, that we don't raise expectations too high.

Social science and ethics stakeholder

3.4 Commercial and pharmaceutical organisations

Overall vision for the science

There was generally a more cautious view from commercial stakeholders with regard to the potential of stem cells which were described as 'not the panacea everyone thinks they are'.

Despite the challenges involved, it was agreed that advances were possible in stopping uncontrolled cell division and that there was potential to use stem cells and tissues for regenerative applications. Coupling stem cell research with developments in nanotechnology, particularly through advances in nano-scaffolds, was also seen as promising.

Respondents were sceptical of the potential for individualised therapies, and more broadly the cost of regenerative medicine preventing wide access to treatments and availability through the NHS.

Private sector respondents were also sensitive to the wider ethical consequences of the science and were keen to ensure that any developments in the field had the buy-in of the public.

Research, regulation and funding

It was acknowledged that the UK had done well in the past few years in becoming a world leader in stem cell research and had attracted many outstanding scientists – though overall it was still seen to have a skills shortage.

However, a number of countries were now seen to have closed the gap on the UK's advantage, and respondents were concerned that significant investment in therapy development was now needed if the UK was not to fall further behind. In this regard, the level of funding by the UK Government was seen as very low compared to the picture internationally.

It was noted that the lack of a coherent international regulatory framework, both in Europe and globally, was likely to hinder commercialisation. There was also concern that as new therapies could be classed as either medical devices or therapies, there would be different regulatory pathways through the European Medicines Agency (EMEA) or MHRA. There were also seen to be challenges in whether the procedures set up for medical devices were adequate to govern complex live cell products. Another key concern for regulation in the UK was the perceived problem in getting therapies through to patients - as one respondent noted: *at the moment we have a zero risk system*.

It was argued that strong regulation was needed to build public confidence in the absence of clear tangible benefits from the work. There was a concern that laws governing stem cells should be careful not to overstep moral boundaries, as it was believed that a major controversy in the area could set the science back significantly. The work of the MRC and BBSRC in funding this project was welcomed in this regard.

A further concern was that whilst the principles governing much of the science were effective, the practice of regulation could be bureaucratic - for instance the need to have a permit for each ES cell project was seen as cumbersome, and was not reflected in the regulation of countries such as Sweden.

Embryonic stem cells

When ES cells were considered, the main view expressed was the need for cautious development, and that research in this area should be cognisant of societal views. With regard to IVF, there was a general agreement that 'spare embryos' should be utilised for research purposes providing that consent was gained and adequate governance procedures were in place to ensure that donor rights were respected. However, the creation of embryos purely for research purposes was seen as ethically contentious and certain respondents were concerned about where to draw the moral line.

The most contested area was hybrid research: here views were mixed between viewing advances as fine as long as a good regulatory system is in place; to

questioning whether such work was necessary to progress the science. It should be noted that these concerns were not ethical positions *per se*, but rather concern about a potential public backlash against the science – with certain respondents also reflecting on their organisation's position in this area in relation to the religious right in the US.

There was cautious optimism about IPS cells – on the one hand there was a need to demonstrate they had the same potential as other pluripotent stem cells; on the other there was concern expressed about possible cellular transmission of viruses and infectious agents. There was a view that while both areas of research were needed, over time developments in IPS cells could reduce the need for ES cells.

Tissue-specific stem cells

With regard to tissue-specific stem cells, whilst adult cells were seen as useful for certain applications, their lack of plasticity and costs associated with treatments were major barriers to full commercialisation. However, the potential for neural stem cells to facilitate neuron and brain reconstruction was singled out as a promising area of research.

The other key area highlighted with regard to tissue-specific cells was foetal material. Whilst again conscious of public views, work in this area was seen as promising and there were no objections by any interviewees to using aborted foetuses, providing there was clear informed consent.

Therapies

One of the most significant concerns with regard to therapies was the cost of commercialisation and whether the NHS would be able to afford treatments on a wide scale – precipitating concern that returns on the huge investment needed to develop SC treatments may be difficult. There were also concerns that the costs associated with regulation and developing adequate consent and ethical frameworks would be significant. For instance, it was noted that though hospital ethics committees were well placed to consider the effects of molecular drugs and biologics, they were less effective when considering the use of medical devices, implants and other treatments. As noted earlier, the classification of stem cell advances as either a device or a therapeutic could mean the regulatory pathway will be very different.

In terms of non-therapeutic applications, the use of tissues derived to assist drug screening was seen as a useful development that could potentially contribute to a reduction in the use of animals for testing. With regard to oncology, using stem cells to learn about cellular growth and differentiation would enable development of targeted drug treatments.

One of the most important approaches is tissue-specific differentiation for finding targets, for exploring pathologies and for testing potential pharmacological advances to controlling that pathology. So there's a considerable opportunity in the discovery process – it could transform the core of drug discovery if you had, you know, differentiable neural tissue, kidney tissue and hepatic tissue.

Commercial stakeholder

Overall, respondents were concerned that media reporting of developments in the field and the hype around therapies may ultimately make the delivery of applications in society an arduous process.

3.5 Religious and faith groups

Overall vision for the science

Whilst stem cell research was supported across church groups, those with absolute views on the moral sanctity of the embryo were opposed to embryonic research and focused on the benefits from research on TS cells; those with relational views were supportive of ES cell research into serious conditions and treatments made accessible to all – though were also hopeful that progress would be made in other areas to prevent the need for research on embryos at all.

We are keen to use science and medical technology for the curing of you know these particularly difficult diseases and sicknesses to which at the moment there isn't any cure. But our stand would be any research in this area and any cure should be ethically acceptable, our basic stance is that there shouldn't be in our view research on human embryos because of the sanctity and dignity of human life, and it's not ethical we would argue to treat those embryos as if they are sort of commodities to be sometimes created for that purpose and then cast out after 14 days or whatever.

Religious and Faith Group stakeholder

Overall there were many areas where the science could have an impact on disease and, given the early stages of research, certain respondents were hesitant to highlight particular areas. For others, the treatment of degenerative disorders such as Parkinson's was seen as one area of considerable promise. The hope was that universal therapies could be developed that helped the many and not the few. It was also highlighted that the diseases of the developing world should be targeted.

It was also viewed as important that religious communities help to shape developments in this area, both in terms of scientists entering into public debate with religious leaders, but also in terms of religious representation on ethics

committees. It was noted that scientist should be mindful to understand how developments in their research 'impinge on cultural and religious sensibilities'.

Research, regulation and funding

Respondents with absolute views on the moral status of embryos were concerned about the regulation of the field in the UK and argued for the establishment of an 'independent national bioethics commission'. The HFEA was perceived as a 'closed shop' taking 'ad hoc and permissive decisions' in this area. They were not convinced that legislative developments in the UK on such important ethical matters were undertaken with a proper reasoned debate. For those with relative views on the moral status of embryos, the legislative balance in the UK was about right.

Despite the strong regulation in the UK, there was also a concern expressed around the transparency of research and whether scientists were conducting research out of the public gaze.

You know sometimes how the suspicion that not all is revealed and there is much more going on that you will think. I think that actually is probably out there.

Religious and Faith Group stakeholder

Embryonic stem cells

It was highlighted that the potential of embryonic stem cells for curing human diseases is simply unknown at the moment, and respondents were concerned about the hype around certain aspects of the science. This was not to argue that there would be no benefits from this research – rather that clinical applications were, at the present, 'conjecture rather than fact'.

The future potential of treatments was explored and the ethical trade-offs between the rights of the embryo and the rights of patients discussed.

Yes well I think… the basic principle is it isn't ethical to interfere with human life at however early a stage. Now if in 10, 15, 20 years or whatever some real therapies were produced from this research, again all I could say at the moment, because this hasn't happened yet, that it would raise an ethical question which the Church would need to consider. Because I mean just sort of as a knee-jerk reaction I suppose some people certainly would say no I couldn't use that therapy because of the way it was created. Now I simply don't know at the moment, I mean I hadn't really considered that, and I'm not sure the Church has because nothing has been produced, but it's something which moral theologians I'm sure will now be thinking about so as to give guidance to people.

Religious and Faith Group stakeholder

Respondents who were permissive of ES cell research were also uneasy around developments in the field. The embryo was viewed as not 'human as such … but there is a potential there and it does have sanctity'. There was a specific distinction made between 'cellular life' and 'human life'. As such, on balance the potential clinical benefits for society from ES cell research outweighed these concerns. It was also noted that such embryos would otherwise be destroyed.

I don't personally, but I do recognise that there would be, there are people that would have reservations, mostly pro life or religious in nature and although I come from a faith position, I don't take the view that we should not use.

Religious and Faith Group stakeholder

It was also noted there were different interpretations in texts such as the Koran as to when human life began. Given the advancement of the science, and the fact that ES cells were taken from non-implanted embryos, it was also highlighted that scriptural guidance could only 'be inferred - there would be no categorical statement, because it's a totally new concept altogether'.

A more significant worry was 'harvesting the embryos just to procure the stem cells' – particularly in terms of creating a market which may stimulate trade in tissues.

IPS cells were seen as a significant step forward, particularly by those with absolute views on the moral status of the embryo. However, their overall position was one of cautious pragmatism, given concerns regarding the health and safety of such procedures.

Oh yes, yes, that would be a much more ethical way of doing things. I think however the caution would be sort of pragmatic at the moment, saying well, you know, what are you doing, and you know, can you overcome this thing of the tumours and so on, and what would be the effects, you know, of using such cells or derivatives from the cells, you know, to try and help somebody? But I wouldn't have the same or anything like the same fundamental ethical problem with that.

Religious and Faith Group stakeholder

For other respondents, whilst noting the significance of the research, they were keen that future work should not be done at the expense of embryonic research, despite the ethical concerns in this area.

Tissue-specific stem cells

Research on adult stem cells was generally supported by respondents, being seen to overcome the ethical concerns associated with embryonic research. It was

argued that research in this area should be targeted at the most serious medical problems, and any treatments should respect the autonomy and rights of the individual.

For the majority of respondents, foetal material should not be used for research purposes. However, there were more permissive attitudes to the use of cord blood.

With regard to the umbilical cord, we could possibly be more permissive than with regard to the aborted foetus. See from the Muslims, our understanding is that anything that is on the body should be buried.

Religious and Faith Group stakeholder

Therapies

Stem cells were viewed as potentially treating a range of degenerative and life-threatening disorders,including for skin disease, burns, diabetes, replacement of pancreatic cells, damaged neurones, joint problems and blood diseases. Despite this promise, there was a need to start showing results because 'otherwise people are going to get rather dispirited by the whole field'. There were also concerns that therapeutic applications would be directed to more cosmetic applications.

Access to these technologies within the developing world was highlighted as a significant issue – seen to be driving further health inequalities between the haves and the have nots.

There's going to be an international consequence. The gap is getting bigger. We're getting richer, we're getting more advanced. They're falling behind and becoming poorer. So it's, you know, that's how things are.

Religious and Faith Group stakeholder

It was also acknowledged that ultimate therapeutic applications could not be realised without significant investment from the private sector and also in the infrastructure needed to provide clinical grade stem cell lines.

3.6 Medical charities

Vision for the science

Whilst respondents were hopeful that stem cell research would lead to better treatments, they were also mindful not to raise hopes of clinical treatments being widely available and affordable in the next few years.

There were a number of areas where stem cells were seen to hold promise, including Parkinson's, Alzheimer's, Multiple Sclerosis and Muscular Dystrophy. It

was noted that there were markedly different levels of funding from medical research charities for stem cell research across these areas.

A key principle underpinning the development of any scientific vision for stem cells was the need to embrace the interests of patients. Ultimately, the benefits of research needed to be demonstrated, either in terms of tangibly better patient outcomes or in terms of greater knowledge and understanding. These ends were paramount and, without bearing them in mind, research - particularly on ES cells - was difficult to justify.

Research, regulation and funding

Whilst basic science in the UK was generally considered to be very good and 'leading the field in Europe', it was not seen to be able to compete with the scale of research in China and the US.

Regulation in the UK was broadly supported. There was greater concern that much debate on stem cells was sensationalist – in terms of companies over-claiming that we will have cures in the next few years, to campaign groups using emotive language around the use of embryos. Informants argued for a more dispassionate review of the arguments, for and against, and for empowerment of people so they can make their own decisions.

The relative levels of funding in adult and embryonic stem cell research were highlighted and, though viewed as high at a European level, were seen as being dwarfed by spending in the US.

To ensure that the impact of funds was maximised in the UK, there was a need to ensure strategic coordination between investment from medical research charities, the research councils and the private sector. The work of the UK Stem Cells Funders Forum was seen as an important in this regard, to ensure the overall health of the field in the long term.

Well as I said what we need to do is to have a comprehensive and coordinated approach to stem cells research, with the specific goals with specific aims. I think we have a very general strategy but we need to get some funding bodies to come together and put together a much more structured approach so we know what we want to do and we know how we're going to do it, and within the, obviously within the appropriate legal and ethical framework but also, the ability to re-evaluate as things progress.

Medical Research Charity Stakeholder

There was a significant concern from certain respondents around the ability to translate research into therapies. Private investment was needed in order to assist this translation. However, there were certain concerns as to how

intellectual property rights would be developed. It was also noted that, due to the long horizon before there was a financial return on investments, venture capital funding for treatments would be wanting and long term funding from public and charitable sources was paramount.

Embryonic stem cells

There was support for embryonic stem cell research, though on the whole respondents generally saw ES cells as tools for research which would provide insights into the manipulation of adult stem cells and somatic cells, rather than ultimately leading to therapies in and of themselves. It was strongly stated that research should not be pursued for frivolous purposes - and that treatment of serious diseases should be the core aim of the field.

In this regard developments in IPS cells were viewed positively and seen very much as a continuum from ES cell research.

At the moment a lot of the work is obviously being done in embryonic stem cells I think ultimately what we need to do is to move toward the area where you can reprogramme adult stem cells so that, there again from the point of view from Parkinson's they become nerve cells obviously. That's the way I think we're going but we need to use embryonic stem cells as a tool to understand better how to do this.

Medical Research Charity Stakeholder

Despite it being seen as an exciting advance, concerns were raised about the potential consequences of gene modification in adult somatic cells, which was viewed as more risky than altering the gene expression within ES cells.

SCNT and cytoplasmic hybrids were both acknowledged as useful tools for research in the field, though certain respondents noted they could not see the need for the creation of true hybrids for research purposes.

In terms of the ethics of ES cell research, whilst appreciating concerns, the morality of not treating patients with serious diseases, when there were tools available to gain understanding and develop potential therapies, outweighed these factors:

In my view, in my personal view, the human dignity of almost the million people with Alzheimer's and what they're suffering and their carers is more important than the dignity around embryos that some people are very concerned about.

Medical Research Charity Stakeholder

Tissue-specific stem cells

Developments in AS cell research were valued, particularly the use of stem cells from bone marrow for the treatment of diseases such as leukaemia. A key issue was the capacity of the stem cells to generate the appropriate cell type for the treatment of a particular condition. For instance, it was highlighted that currently there is no evidence that nerve cells can be generated from adult stem cells.

They're not versatile enough. To actually form very specialise cells from nerve cells, whereas when you're talking about you know generating white blood cells or even skin cells which are much less differentiated well you know stem cells derived from bone marrow may be appropriate for that. When you're talking about making very specialised cells - you know neurons for Parkinson's for example, then you need to have a very flexible stem cell type and at the moment the only place you can get that is in the embryo.

Medical Research Charity Stakeholder

However, it was argued that the ultimate goal would be to use the insight gained from embryonic stem cells to understand cell differentiation and to be able to generate pluripotent stem cells from adult somatic cells – avoiding the need for embryos in treatments. This 'Holy Grail' was viewed as a considerable way off in research terms.

There was a pragmatic view as to the use of aborted foetal material, in so much as so long as appropriate consent was obtained, it would be more beneficial to use the tissue rather than destroy it.

Therapies

Respondents were positive around the potential for therapies, and saw early successes most likely come from bone marrow-derived stem cell lines.

It was stated that the therapies most likely to succeed in this area would be an artefact of those with the greatest funding.

There was noted to be a lack of fundable applications for stem cell research in a number of disease areas, for example Multiple Sclerosis. The question of whether there was a large enough pool of researchers necessary to do the work was also raised.

It was also highlighted that it was likely to be very expensive to trial stem cell therapies, but these costs needed to be offset in terms of savings in social care and other treatment regimes, such as enzyme replacement therapies.

There were a number of significant concerns noted with regard to treatments, including the transmission of infective agents and tumour growth. However, it

was noted that for many degenerative conditions, SC treatment will be an improvement because there is no effective current treatment. The greatest challenge is hence balancing these risks against potential benefits in the context and setting of informed consent.

In terms of moving into clinical trails, one respondent noted that general ethics committees currently in place cannot cope with the specifics of different stem cell applications and that a specialised ministerial advisory committee may be required, especially around the translation to clinical trials.

Finally, the need for greater communication between scientists and clinicians was highlighted, both to clarify the aims of research and to consult with those who may eventually be using the stem cells in clinical situations.

3.7 Pro life groups

Overall vision for the science

The key vision for stem cell research involved the use of TS cells to develop treatments, and that any progress in science should have absolute respect for the dignity of the human embryo.

Overall, providing that embryos were not used, respondents welcomed any stem cell research that would find means of treating and curing diseases, alleviate human suffering and improve patient care and quality of life:

We're not opposed to stem cell research per se. We fully support the use of umbilical cord stem cells and adult stem cells. We're only opposed to the use of embryonic stem cells, and we are encouraged by the progress that's been made in the use of stem cells from what we would consider to be ethically acceptable sources.

Pro Life Stakeholder

Respondents were unconvinced as to the necessity of ES cell research, principally on ethical but also on safety grounds. It was argued that research was driven by scientists 'who don't want to accept any restrictions on the work that they're doing' and that the public were manipulated by the media hype surrounding 'potential cures'. It was argued that stem cell science should be about finding the simplest way forwards, not the most convoluted.

Research, regulation and funding

While UK science was highlighted as strong, for certain respondents it was argued that it would be difficult for us to compete internationally given the levels of funding in the US and Asia.

I'm really quite amused by little Britain really. It's like a tiny little country claiming to be at the forefront of everything, and you've only got to see the stem cell budget for California to realise that it's in our dreams that we're going to outpace the American dollar. I think that I would like to see the United Kingdom a little bit less obsessed with we're leading the way and really do more robust investigation into what we're actually doing.

Pro Life Stakeholder

Rather than attempting to be a world force in stem cells, efforts should be concentrated on improving the regulatory regime. Specifically, it was argued that the debate surrounding legislation and regulation in the UK had been polarised in favour of embryonic research. It was argued that regulators in the UK were too strongly aligned with the scientists' viewpoint, were untrained in considering the wider social and ethical implications, and did not adequately represent the views of the public. Decisions of such a controversial nature, it was stated, should not be made by a small handful of people.

A different form of governance was argued for, with greater reflection on ethical issues and greater accountability of regulators such as the HFEA. It was argued that science was often progressing too quickly without the institutions catching up and without the necessary time given for reflection on the type of society we create though stem cell developments.

Finally, in terms of investment, it was noted that treatments would not be funded without the involvement of the private sector. It was argued by certain respondents that in the US, the market had reached a different conclusion to UK public funding by funding adult over embryonic research, as that was where there was most potential.

Embryonic stem cells

Respondents were against any research on embryos for any purpose other than to benefit the embryo itself. The destruction of the human embryo was believed to be morally wrong - as life was viewed as beginning at the point of creation. The view was that if an embryo is created under any circumstance, then the embryo automatically acquires a moral status.

Well we're opposed to any research using human embryos. We have absolute respect for human life from the moment of conception, from the moment of the one cell embryo, and so any destructive research is something we would oppose, any deliberate intervention which destroys the human embryo, we would be opposed to.

Pro Life Stakeholder

It was also argued that ultimately, due to the difficulties involved in controlling cell differentiation and in terms of immune response concerns, ES cells were more likely to be used as research tools rather than for therapy. One respondent stated that they were advised on scientific grounds that ES cells could never be differentiated into the desired tissue type that could be used *in vivo* – whereas adult cells were intrinsically suited to such as task.

There were also significant concerns around the use of SCNT, with certain respondents believing that research into this area would involve the exploitation of human beings. It was also argued that the processes were extremely unsafe and that much of the history of animal cloning had been largely hidden from public view. In this light, hybrids were also seen as an 'unnecessary complication' to the debate and should not be permitted.

Leaving aside our absolutes on these things, there's also the issue that the history of cloning in animals has been so appalling so… and I think a lot of it's hidden too from the public. I think if you showed a few pictures of the horrors that have come from animal cloning to the public, they'd probably wake up a bit more about the implications. I mean, you know, it always feeds back to the issue of necessity. How much messing around do you have to do? My vision of science is that it's not about finding convoluted difficult ways to get to the end goal; it's looking for the fastest and the simplest way forward, and I think that the proposals at the moment, when you include cloning in animals and hybrids and all the rest of it, you're just asking for trouble at every step of the way.

Pro Life Stakeholder

More broadly in relation to hybrids, it was argued that there was a 'race to the bottom' in the UK, with licences granted for research that was deemed unacceptable in other countries.

On the whole, IPS cells were welcomed as an advance, and a distinction was made between ES cells and those derived from adult somatic cells. The main criterion was that such techniques would only produce stem cells and tissue lines, rather than a viable embryo-like entity that could lead to the creation of life. This withstanding, the research was supported. One respondent thought that developments in IPS cells were of major significance and would 'really transform the debate'.

Tissue-specific stem cells

Research on AS cells was generally welcomed – indeed it was argued that there were already a large number of treatments derived from adult cells which were benefiting patients, in stark contrast to embryonic stem cell research.

There were concerns across all stem cell science about the pace of developments and the rush to get to treatments – and that patients should not be exploited through the use of experimental treatments.

Whilst noting some of the clinical limitations for AS cells, it was argued that no therapy should ever require the full range of potential cell types, and working with AS cells either nearby or in situ offered the greater potential.

Then I ask you, why do you want the full range? If I've got spinal cord injury, I don't want the full range; I want the spinal cord repaired.

Pro Life Stakeholder

There was concern that AS cell research did not attract enough investment due to difficulties culturing them *ex vivo*, leading to expensive treatments.

While research on foetal material should not be permitted under any circumstances for certain respondents, others argued that when such tissue was derived morally, for instance if foetuses had 'died naturally' through miscarriage rather than through abortion, and providing there was consent, then such research should be permitted.

Cord blood was seen as having great potential for certain respondents - due to their 'proximity' to embryonic stem cells, and a belief that they would have greater plasticity.

Well the reason that I love the cord blood stem cell, is because of its proximity to the embryonic, so it has the good qualities of the embryo without the ethical problems, so I'm using the cord blood stem cells that I believe will also be… you can get similar cells from the placenta, from the amniotic fluid and all kinds of areas in very early life, and of course, this is the aim, to try and create the embryonic like stem cells without destroying the embryo, so I think this is the most exciting area of stem cell development because they do have greater versatility.

Pro Life Stakeholder

Therapies

Overall it was envisaged that stem cells would be useful in treating and curing some debilitating diseases.

As noted above, for certain respondents, cord blood was viewed as an area with great potential. It was also argued that around 80 conditions were currently being treated with cord blood stem cells, but it was under-funded due to the 'sensationalist headlines' generated by embryonic research.

It was also argued that stem cell treatments of any nature were likely to be very expensive, and as such there needed to be an 'ethics of investment alongside an ethics of embryo research', and the public should play a full and informed role in the shaping of technologies in the future.

Finally, it was noted that in the rush to develop stem cell therapies, alternative routes to treatments may be ignored. It was argued that there needed to be a greater focus on preventing disease in the first place, understanding conditions and addressing causal factors.

While certain areas of stem cell research were seen to have great potential, it was argued that there 'is a risk that it will be focused on to the detriment of other approaches'. In this regard, the individual with a disease should be able to say 'I don't want stem cell therapy' and still expect the best care.

3.8 Funders

Overall vision for the science

Regenerative medicine was seen as having a major impact in improving patient quality of life and addressing the diseases of ageing. Respondents were keen for research to be relevant and responsive to societal needs – there was a particular need to ensure structures were in place to facilitate the translation of basic science to therapeutic applications.

I think that there's a lot of talk these days about translation from basic science through to support for the patient, and I think that although it might sound a small issue, it isn't a trivial issue; what that means in practice, and I think what that has to mean is really strengthening various steps of the pipeline that go all the way from, if you like, basic research through to, you know, therapy and prognosis, and that includes issues like training.

Research funder stakeholder

Certain respondents thought that progress was likely to be made through the manipulation and differentiation of existing stem cells in tissues, rather than through regenerative transplants. There was also the potential for differentiated stem cell lines to be used for drug screening. There was particular excitement with regard to stem cell developments in at the interface with bio-nanotechnology. However, this was tempered by the concern that enthusiasm around the science could create unrealistic public expectations – the need for 'hope not hype' was advocated by respondents.

Research, regulation and funding

Overall, the UK was viewed as having a relatively strong research base in adult and embryonic stem cell research compared to other countries. When funding was discussed, the primary concern was not around the levels of funding *per se* - the limits to which were not thought to be holding back research - but rather that money was spent wisely on high quality work. A significant concern was the limited number of very good researchers attracted to undertake work in the UK.

Overall the UK's legislative framework, together with generally supportive public attitudes, was seen as a positive creating a positive environment for stem cell research relative to the US. Scientists engaging in dialogue with the public were viewed positively and there was seen to be a complementary relationship between such engagement and the development of effective regulation.

I think scientists are pretty sensitive to issues, you know, public issues and legislative issues, and I suppose being a scientist… you know, people aren't sort of sitting in their labs making monsters. The important thing there is that there is an engagement, that the legislators engage with the community, the scientific community as well as the general public, because I think otherwise, the danger is that you end up with inappropriate legislation, which either stops appropriate development or, you know, just is irrelevant.

Research funder stakeholder

Embryonic stem cells

In terms of the science, one of the key issues was related to the expense of generating embryonic stem cell lines and the need to collaborate internationally to help guide research and investment in this area. Investment needed to build on UK strengths.

Key research challenges included how to control the growth and differentiation of ES cells, how to mitigate the potential for tumours, as well as how to ensure the safety of treatments and prevent the transmission of diseases in therapeutic applications. IPS cells were seen as a major development and, though the research was in its infancy, would now lead to significant international effort in this area. In particular, engineering stem cells in situ was seen as a way forward that could overcome the ethical concerns related to ES cells.

You know, it could be that people move away from the idea of embryonic stem cells and move towards a much more engineered situation. I think that actually finding out how you get stem cells in situ to differentiate, so things you could add in a particular situation to get the remaining stem cells or tissue or whatever, to grow and differentiate; I mean that itself, you know, would get round many of these problems and would be a huge way forward.

Research funder stakeholder

In terms of ethics, respondents were content that the degree of regulation in the UK adequately addressed ethical concerns and provided scientists with a licence to practice. Ultimately, embryonic stem cells were seen as a tissue source and, as these would never be implanted, many of the moral concerns were circumvented. However, it was acknowledged that there would be problems if a market for embryos is created.

It is about strict ethical guidelines and appropriate ethical procedures, there is nothing intrinsically wrong with either of those processes [IVF and PGD] at the moment. If, there becomes a market, it becomes unpleasant and unsavoury.

Research funder stakeholder

Tissue-specific stem cells

AS cells were seen as having value due to their public acceptability and in terms of overcoming tissue rejection issues when used in autologous treatments. The combination of innovations in AS cell science, together with bioengineering and nanoscaffolds was seen to be where breakthroughs in organ, joint or tissue replacement may come. Notwithstanding this, it was again stated that there was much fundamental research to do in this area, though near term therapies were more likely than in ES cells.

Therapies

Whilst respondents foresaw advances in the therapeutic use of stem cells to treat degenerative eye diseases and some neurological conditions, overall breakthroughs, particularly in the field of ES cells, were some way off. As one respondent noted:

If you asked me where is stem cells going to be in ten years time, I suspect we are still going to be predominantly in a petri dish and in a culture flask rather than in a patient.

Research funder stakeholder

Again, the public value of stem cell research was highlighted and, given much of the research focused on tissue repair, respondents were keen to highlight the need to ensure applications improved the 'productive lifespan of a population'.

There were significant concerns around the potential for terratomas and immunological complications to hinder developments in the field.

A key barrier to the development of stem cells was limited investment of pharmaceutical companies in regenerative medicines – the innovation pathways

of such organisations not well set up to produce live cell-based therapies. It was argued that differentiated stem cells could be very important at various stages in the drugs development process and it was here that most interest from pharmaceutical companies would be in the first instance.

3.9 Government and regulators

Vision for the science

Views were mixed with regard to the prospect for stem cell research – certain respondents viewed it as offering a transformative approach to dealing with degenerative diseases; others offered a more downbeat assessment, believing it was very difficult to predict ultimate clinical benefits, and saw applications in the near term with regard to toxicology testing for new drugs and in terms of better understanding cancers.

All respondents agreed the timescale in moving from the laboratory to clinical practice was uncertain – and that there were significant clinical risks that needed to be overcome. Overall there was seen to be the need to allow basic research to continue on all varieties of stem cells sources.

In addition to the potential health benefits, the economic implications of treatments were also highlighted by certain respondents – which, though high in the short term, could potentially save significant NHS resources with regard to social and palliative care.

Research, regulation and funding

There was a positive view of UK science, which had built on existing strengths in developmental and reproductive biology. The regulatory framework was also highlighted as being very effective, seen as driven by clinical rather than political needs, with certain respondents stating the UK was the world leader in this field.

So we sometimes forget that though we are a small island in terms of our basic science we are regarded as ethically incredibly responsible. So I think in those terms we do lead the world. I also think that because we have taken this very strong regulatory approach where there is an independent regulator with, that has got public confidence where we have researched council funds which are independent of government actually funding research given very very clear ethical guidelines, what we do have is a sort of an ability and an objectivity about our research which you don't have in the United States, which you don't have across most of Europe.

Government and regulatory stakeholder

One of the key issues with regard to effective regulation was considered to be that both the law and the institutional structures were in place that would enable

the creation of embryos for treatments and not just for research purposes, particularly as research moves into clinical trials phase. This will involve coordination between the HFEA, the HTA and the MHRA, as well as engagement with the scientific community to ensure such development is effective.

I think it's important that the scientific community is engaged with that process and ensuring that when the time comes to move towards, you know, moving towards therapeutic use of these products and what the development of these products is themselves through clinical trials that the regulatory mechanisms are going to be effective and not slow up the development.

Government and regulatory stakeholder

There was a view that overall public funding for research was adequate, though not on the scale of investment in the US and Asia. It was also viewed as important that reasonably substantial public funding be maintained so that treatments were not solely driven by markets and could ultimately help benefit 'the many and not just the few'.

More broadly, the economic benefits from successfully commercialising stem cell treatments were thought to be significant – for instance the UK was near to clinical trials for a stem cell therapy for Age-Related Macular Degeneration, which if successful would potentially have a large global market.

Certain respondents were also concerned that regulation should not be 'putting a block' or disadvantaging UK commerce, providing the overall governance was done in an open and transparent fashion. Conversely, respondents were also concerned about the amount of investment in research needed from the public purse to bring successful treatments to fruition.

There was a need for the scientific community to be actively involved in policy making to ensure it is well-informed, robust and where possible future proofed – generally respondents felt that such engagement was good and effective. One respondent highlighted that there is a lack of a coherent ethical framework for the consideration of stem cell developments.

The big problem here though is the lack of a proper ethical framework in the UK. We do, we do lack either a National Ethics Committee which I would prefer Parliamentary ethics committee and the need for a standing parliamentary ethics committee which can advise government, not just simply on this issue but on other emerging ethical issues, you know I really do think is a weakness in the system.

Government and regulatory stakeholder

Building on this, scientists were key in building trust with the public which was a prerequisite for effective regulation. Given the speed at which the science moved on and its complexity, ultimately systems of regulation needed to be trustworthy and scientists need to be seen to be behaving acceptably. The role of public engagement was central to this, in helping to create the environment through which scientists' licence to practice was affirmed.

Well I think I think there is no doubt that we are at the moment moving into areas of medical science which are incomprehensible to the vast majority of the public. You know you can't you can't explain the complexities of the science that is going on. Therefore you have got to develop a method whereby the public feel confident that the scientists are being regulated and are behaving acceptably. Now government has a difficult time actually achieving that. It is the scientists who have to achieve that. And so I think that getting public engagement is absolutely crucial if the scientists are going to be able to continue with if you like the blue skies work.

Government and regulatory stakeholder

Embryonic stem cells

Whilst the long term aim was to try and find cures for serious diseases, one of the key issues for ES cells was viewed as understanding the processes of cell differentiation and control.

In terms of the ethics, the early stage embryo was not seen to have a moral status by respondents: it was viewed as essentially a cluster of cells, though sensitivities surrounding such debate in this area were acknowledged as significant.

I think once you have a cavalier attitude to the material which is human material then I think you start to undermine public confidence. So it is important if you like the dignity of any human material but particularly of embryonic material is always at the regulator's mind.

Government and regulatory stakeholder

Related, the purpose to which research was directed in this area was all-important - concerns were expressed around the potential for 'a face cream rather than a treatment for diabetes' to be developed.

However, advances in the field were seen to precipitate major challenges for regulation and informed consent – particularly in terms of the development of different treatments from embryonic stem cell lines and governing the purposes to which research was put to. The definition of what constitutes a serious disease

was also challenging – and the testing of such cases in the oversight of stem cell usage could be very costly and time consuming.

As more and more applications of stem cells come to the fore, embryonic stem cells, it's going to be difficult to really control every aspect of how they're used and, you know, a good argument came out a while back about people using embryonic stem cells to study deafness and someone challenged whether deafness was a serious disease. Well it starts to get really complicated when you talk about purposes and what someone's perception of a serious disease and the other person's perception of a serious disease is.

Government and regulatory stakeholder

The use of spare embryos from IVF was seen to be permissible with consent. However, certain respondents thought that there may be a move away from the use of spare embryos towards the creation of embryos specifically for research purposes, by various means.

The legislative process around hybrids was discussed at some length. It was argued that in developing the legislation, public opinion, the ethical issues and also the legal issues were taken into full account.

IPS cells were noted as a remarkable development in the science which 'could change the landscape for stem cells'. Whilst the UK is well placed to contribute to IPS cell research, it was thought that it could lose the lead to Asian countries or the US. More broadly, such advances meant that the ethics in this area were constantly in flux. Changing science led to changing public debates and it was important that the governance of this area was responsive to such concerns.

That's going to have huge implications on stem cell research. That wouldn't have even been predicted even 6 months ago by any of the scientists because it turns out it's quite…, you know, relatively simple to actually reprogramme them back and most people thought it would be a very complex process to do that. But the ramifications for that are very big.

Government and regulatory stakeholder

Tissue-specific stem cells

Clinical developments were acknowledged to emerge from research on AS cells in the first instance, though there were thought to be significant issues in developing widespread clinical use due to problems in culturing such cells.

Overall, in investment terms, there was not seen to be a major need to distinguish between AS cells and ES cells in terms of picking winners – rather than significant advances were likely to arise from shared insight from both fields.

There was a strong view that research into AS cells needed to be funded alongside ES cell research.

It was also noted that the HFEA did have any 'regulatory bite' in AS cell research, except to consider the necessity of embryonic research.

Therapies

There were a number of therapeutic areas where stem cells were viewed as having an impact, including repairing skin and muscle tissue in the near term, and longer term in treating neurological conditions, though it was noted there would be significant ethical challenges in developing clinical trials in this area.

It was also argued that even though therapies will be some way off, funding in this area would 'deliver a lot of science', which would inform research directly in the field and beyond.

However, respondents noted that there were significant challenges in getting to effective clinical treatments, particularly concerns around tissue compatibility leading to adverse immunological reactions, and issues in the control of cell differentiation leading to potential tumours and malignancy.

Certain respondents cited problems in gene therapy and were keen to ensure that such issues did not arise again in stem cell treatments.

With regard to drug development, it was noted that there was great potential to use tissue lines created from stem cells for toxicity testing, but this was unlikely to replace the need for animals in research.

One of the key issues related to the production of stem cell lines was keeping track of possible future uses and rethinking what informed consent might mean. For instance, respondents were questioned as to whether ES cells should be used for things that were not originally considered in consent agreements. It was acknowledged that this becomes very complicated when considering uses involved in stem cell banking.

A final concern was around equity and access to therapies in the UK - that treatment was free and at the point of need. There was seen to be the need to build therapies into the NHS – though in reality this was recognised as very difficult as the demand and costs for such treatments were likely to become 'astronomical'.

4 Conclusions

When considering findings, five main themes emerge that are of specific interest for research councils and other decision makers. They are:

- The **value of basic and applied research**, in terms of the development of stem cell science, the ultimate uses to which stem cells are put, and tipping points through which public support is mediated;

- The **ethics of stem cell sources**, in terms of how the ethical debate is framed through the production and use of tissue-specific and embryonic stem cell lines;

- The **investment in stem cell science**, in terms of the role of public and private funding in developing the science, and ultimately the public value that such investment needs to derive;

- The **governance of stem cells**, in terms of understanding the perceived value of legislation and regulation, and the systemic way in which the direction and control of science is shaped;

- The **future role of public dialogue**, in terms of considering what sort of debates and under what conditions stem cell research should be encouraged to advance.

Each will now be explored.

4.1 The value of basic and applied research

One of the most striking findings was the very **high levels of support** for stem cell science and technology. All groups, from public to stakeholders, saw significant benefits for society in terms of potential treatments. **However, support was conditional**.

This conditionality has been well rehearsed in many cases – most notably the distinct support for the use of tissue-specific stem cells, in particular adult and cord blood, over embryonic stem cell research for those members of the public and stakeholders that held strong and often absolute views on the moral status of the embryo.

However, there were conditions placed around research from all participants – both public and experts - which were fundamentally tied to the sources from which stem cells were derived and the ends to which they were placed.

These conditions can be viewed as a series of tipping points wherein support for stem cell science is shaped. It should be noted that such points are not static, but rather are mediated as the science and the social context surrounding developments change. This complex picture, which has implications for how the science develops in the future, is described next.

For public participants within the dialogue, the ultimate uses of stem cells were valued. Undoubtedly the most significant driver was the potential of stem cells to treat serious diseases, particularly life threatening, debilitating and degenerative conditions for which current treatments were of limited therapeutic use.

The necessity to use stem cell treatments only for serious diseases was stressed. This was not only due to the ethics of using embryos, and hence the means justifying the ends; but also due to patient safety and the uncertainties around stem cell science at this early stage.

However, **what constitutes a serious disease was contested**. Whilst at one end of this continuum diseases such as cancer, Alzheimer's and Parkinson's, together with serious injury, were viewed as worthy areas for research; at the other end, cosmetic applications such as face creams were not. However, there were many applications such as the growth of new teeth or treatments for acne or baldness that were more contested – though generally considered not to be serious enough to merit use of embryonic stem cell lines.

There was a far more complex set of discussions around the treatment of diseases such as diabetes. In these instances, there were mixed views as to whether such research should be permitted in these circumstances for a variety of reasons, particularly the effectiveness of the current treatment regime and risks of the treatment.

This was further complicated when considering the needs of different patient groups – for instance whether treatments should be targeted towards the diseases of ageing versus treatments for conditions that affect younger people.

Support was shaped by motives for research - for instance there was resistance to the use of stem cells for the purposes of human enhancement. It was also shaped by the wider implications of technical innovations, such as SCNT leading to the potential for human reproductive cloning.

These concerns are of more than ethical significance. They raise particular challenges concerning the future of support for stem cell science, as issues such as what constitutes a 'serious disease' or even what constitutes an 'embryo' (as certain stakeholder groups hinted at with the development of IPS cells) become contested.

They also forge particular issues for the governance of science – not only how to develop adequate procedures of informed consent around future uses of stem cell lines; but also in terms of the type of society we create with the possibilities that the science offers us. As funders of research, the BBSRC and MRC are not passive observers of this process. The adequacy of governance structures to deal with these issues is discussed in more detail below (see 4.4 and 4.5).

In addition to the curative potential of stem cells in the treatment of diseases, from a public perspective, other significant drivers for the science were their use for understanding diseases and for diagnosis. In particular, treatments that empower people to take control of their health were valued.

Building from this, and in relation to the uncertainties around the science, **the role of basic research was increasingly valued by public participants over the course of the workshops**. Whilst the ultimate ends of research certainly needed to be kept in mind, understanding cell differentiation and control were thought to be a high priority.

This framing of the purposes of stem cell research was particularly evident in the expert interviews. The predominant focus in many of these discussions, particularly for those with a technical knowledge of the area, was not concerned around treatments per se, but very much around the need to improve our basic understanding of developmental biology.

There was a plurality of perspectives amongst all stakeholder groups as to the therapeutic ends to which stem cells would be directed and their ultimate clinical efficacy. This ranged from predominately seeing stem cells as a tool for understanding diseases to one where there would be variety of clinical applications from embryonic stem cell lines within the next decade. Indeed, many stakeholders questioned whether ES cells would ultimately be used in treatment, or whether developments in IPS cells would ultimately lead to the ability to manipulate cells *in situ*.

There was a disconnect between these 'private' conversations and the wider media and public debate on stem cells in the UK, which often focused on 'miracle cure' headlines. This tension was picked across a number of stakeholders in terms of 'hope not hype' concerns. Moreover, it was highlighted by social scientists that **the culture of science often made it difficult for individual researchers to voice concerns over uncertainties and risks, making open discussions difficult.**

Whilst these issues were to some extent overcome during the public workshop discussions, the sheer complexity and differences of opinion both within and between stakeholder groups was notable.

A key implication therefore becomes how we talk about **how we talk about uncertainties.** This is not an academic point: it is precisely the manipulation of uncertainty surrounding stem cells which is where the debate takes place. The most notable instance of this was the propensity to over-claim benefits and under-claim risks in relation to private firms collecting and storing cord blood. But more generally, this tension was seen in the discussion of all areas of the science, particularly in terms of the benefits from ES cell research and IPS cells.

What the dialogue demonstrates is that while therapies are undoubtedly important, **the public are capable of appreciating the value of research, of having complex discussions around scientific uncertainties, and helping to consider social consequences.**

People were supportive of a plurality of research – both basic and applied: stem cell science was not just about picking winners. A mature debate that makes the case for basic research, as well as its uncertainties, will be important for the science to progress in this area.

4.2 Stem cell sources: framing the ethical debate

The sources of stem cells - and particularly the moral status of embryos – have been at the heart of much of the stem cell controversy over the past decade.

Whilst the moral status of the embryo was a significant factor in much of the public discussions, overall it was one factor among many, with concerns around the collection of women's eggs and clinical ethics being as, if not more, important for many participants.

This is not to denigrate the ethical significance of using ES cells – which was highlighted in particular when considering the clinical purposes of research. Whilst for certain stakeholders, and a small but significant proportion of the public, the embryo was viewed as having an absolute moral status, for the majority of participants, a more relative or situational ethics was dominant – shaped by the external context, rather than an immutable set of values. Again, this is significant due to the conditional support for stem cell science outlined above.

These characteristics of participants were highlighted in the Q-method process (see appendix 4) – which broadly typified three groups of public respondents who took part in the process, in terms of their attitudes to stem cells:

Confident supporters - who emphasise the enormous benefits that the research promises, supporting the use of stem cells for basic as well as for therapeutic research, and rejecting various ethical objections to the use of embryos.

Selective acceptors - who reject the use of embryos under certain but not all circumstances, and endorse the use of adult stem cell research and the collection and storage of umbilical stem cells.

Pro life critics – who hold the view that life should never be created to grow spare parts for another person and indeed that embryos, however they are sourced, should not be used for research purposes at any stage in their development.

These different perspectives need to be borne in mind when considering the issues associated with the different sources of stem cells discussed next.

In terms of tissue-specific cells, **adult stem cells were one of the least controversial sources**, particularly due to the view that individuals either involved in the donation or clinical use of AS cells have given their consent. The **principal concerns around adult cells were clinical**, concerning their limited plasticity, and difficulties in growing cells *in vitro*. These clinical issues however had ethical dimensions: plasticity concerns were seen to limit the clinical reach of AS cells, so that certain, particularly neurodegenerative diseases could not be treated through this route (dopamine neurone cells to treat Parkinson's for instance); lack of ability to culture AS cells presented issues for the costs and availability of treatments – a significant concern given that the principle of universal access was strongly endorsed by all groups.

Cord blood use was generally viewed favourably by public respondents and highlighted in particular by those opposed to embryo research. There were, however, **ethical concerns** in this area. The first related to the **collection of cord blood** at birth and the need to ensure the mother and baby were not put at risk. The second related to the tension around **public and private banking of blood**, and the potential for people to be exploited by the commercialisation of this area. The third, and related concern, was that the **storage and handling of cord blood** was clinically safe, particularly in the private sector, and that this area had due oversight from regulators. The final issue concerned overall **clinical utility** – and how clinical properties ascribed to cord blood were used for different purposes, including commercial and ethical. For instance, views ranged from cord blood already being used for over 70 treatments; to one where the quality, number and plasticity of the derived hematopoietic cells meant they were used for only a limited number of conditions – mainly related to childhood cancers, rather than for general clinical use. Notwithstanding this, participants felt it was the right of people to store cells in private banks, despite concerns that a two tier health service would develop if such treatments were to become available.

Foetal stem cells were the most controversial of the tissue-specific stem cell sources. For certain participants and stakeholders this was due to the view that any use of aborted foetuses was morally wrong. However, **the bigger**

concern for the majority of respondents related to the issue of consent, the sensitive nature of any discussion involved and the potential exploitation of women. There were concerns that women should be able to specify the broad uses to which foetal material was put - including for stem cell research. This issue, which was also raised in relation to the use of embryos, is likely to complicate the consent process, conflicts with the current Polkinghorne guidelines[3] and may forge significant issues for the governance of the science in the future. Finally, as changes in the clinical utility of foetal stem cells will impact upon their demand, the potential to stimulate a market in foetal stem cells was highlighted.

In terms of ES cells, the predominant discussion centred on the use of spare embryos from IVF. It should be noted that approximately three-quarters of the public had permissive views on the use of embryos in this regard, a view that increased as people understood the relative development of a blastocyst compared to other Carnegie stages, and the very tight regulation of this area. As noted above, these participants were only supportive for the use of embryos for serious diseases.

This withstanding, a significant proportion of participants were opposed to the embryonic research. For these participants, together with pro-life groups and certain religious stakeholders, human life began at the point of conception and it was morally wrong to use embryos for clinical purposes. A counter view, articulated most clearly by medical research charity stakeholders, was that the ethics of embryo research needed to be offset against the ethics of not treating patients suffering debilitating illness – particularly if the embryo was only to be discarded.

An equally significant issue for many participants with regard to IVF concerned consent around the donation of embryos. Following similar concerns with regard to the use of foetuses, there was seen to be a need to ensure that consent was fully informed, that embryos were used for agreed purposes only, and that there should be no payment for donation. The clinical risks to women were also a concern and, as such, the donation of embryos purely for research purposes was more contested, though again it was supported by the majority of participants, providing consent was sought.

The final set of ethical issues around ES cell lines developed from IVF was the safety of treatments. It was viewed across public and stakeholder groups that there may be major issues in the development of therapies, primarily concerning

[3] This issue was also highlighted in Pfeffer, N and Kent, J (2006). Consent to the use of aborted fetuses in stem cell research and therapies. Clin Ethics; 1:216-218

the establishment of terratomas and the potential for cancers through the effects of undifferentiated ES cells, together with significant immune response issues.

With regard to SCNT and hybrids, while they were viewed as ethically contentious areas of research, they were not seen to be key drivers in the debate by the majority of stakeholders, despite the recent controversies in this area.

For public participants, SCNT was the least supported area for stem cell research. It was seen as having many of the same concerns as IVF, insofar as it still required women's eggs; that the consent process would be made all the more difficult given the social connotations of cloning; and the potential for women to be exploited in this area. There were significant health and safety concerns highlighted, not least related to current levels of efficiency in this area, together with concerns around the potential to facilitate human reproductive cloning. SCNT was noted, by scientific stakeholders, as an interesting area of research, with recent proof-of-concept work in non-human primates seen as significant. However, commercial stakeholders were more sceptical as to where this avenue of research was leading in terms of therapies – and the potential for patient-specific therapies through this route is a long way off.

With regard to cytoplasmic hybrids, after overcoming initial 'yuk factor' reservations, members of the public were generally supportive of this area of research – predominantly as it overcame the need to use women's eggs and the associated issues outlined above. There were a number of conditions attached to such consent, namely that hybrids were used for research purposes only, they were destroyed 14 days after their creation and should only be used for research into life threatening diseases, rather than for cosmetic purposes. It should be noted that there were significant concerns that scientists would be tempted to push the boundaries of this area and undertake research out of the public view: trust, openness and transparency were therefore fundamental.

From a stakeholder point of view, hybrids were also contentious. The scientific necessity of this area of research, though noted by certain researchers, was questioned by others. The recent debate was viewed by certain religious and pro-life groups as illustrative of 'regulatory capture' - with the HFEA being too closely aligned to scientific interests. Certain commercial stakeholders questioned the merit in pushing such controversial areas of science, promoting a potential backlash against the whole area, given the ultimate research utility. However, notwithstanding these reservations, the majority of stakeholders and the public were ultimately permissive of research in this area and keen not to close down potential avenues of knowledge.

Finally, **IPS cell research was seen by stakeholder groups in particular as a potentially disruptive rather than incremental innovation in stem cell science.** A number of groups noted that it had the potential to lead to new forms

of treatment; circumvented the need for embryos; or provided new tools to understand developmental biology. Certain stakeholders noted a degree of hype around the area and that there were significant health and safety issues that needed to be overcome – in particular, the risks associated with gene modification. Whilst the public were generally excited by the area, they were also conscious of the potential clinical risks. It was noted by certain stakeholder groups that stem cell research has not had its 'gene therapy moment yet' – as such, caution was advocated when proceeding with IPS cell research, as unsuccessful clinical trials could cause significant damage to the field as a whole.

At the heart of all of the ethical dilemmas around stem cells was how to make choices in society. There was a tension between a libertarian view, which highlighted an individual's right to make choices around stem cell uses – with patient autonomy fundamental in this regard. The counter view was communitarian – and concerned the need to balance individual rights and interests with that of the community as a whole.

Overall, the libertarian view was far more dominant in the workshops – evidenced by the favouring of people's rights to store their cord blood, or take a risky treatment or donate human eggs for research – despite the wider societal consequences of this. A more communitarian view was evident on a number of concerns around cosmetic treatments. However, in many instances where a more restrictive view on the governance of stem cells was argued – the payment of donors or patients in clinical trials for instance - at heart the main concern was the impact of payment on individual autonomy to make free choices, rather than the impact on society more broadly. As noted, what really constitutes a free choice given uncertainties, social pressures and the hype around the science, is complex.

This tension is of importance to the governance of stem cell science. **There needs to be consideration as to when individual choices should shape science and technology, and when societal concerns, even when not held by the majority, should have more sway**. One of the concerns around the debate - as expressed by church groups and pro life groups, and acknowledged by certain government stakeholders was the need to ensure ethics were taken into account in shaping this area. Governance, and the role of different voices in this process, is explored in section 4.4 and 4.5 below.

4.3 Investment: commercialisation and public value

Greater investment in stem cells was viewed as critical to take innovations from the laboratory to the clinic. Stakeholders, in particular, highlighted the gap between investment in the UK and a number of countries such as the US and China. There was a significant role seen for private, public

and charitable investment if the UK is to successfully commercialise innovations in this area.

From the perspective of the public, private investment was potentially the most controversial issue in this regard. On the one hand, the public viewed private investment as necessary to bring products and treatments to patients. On the other, there were significant concerns around how commercial interests would shape and control the science.

It should be noted that the nature of this concern was not that private sector investment was inherently bad and public investment good. But **the involvement of the private sector was seen to raise new questions about both the means and the ends of research.** Participants expressed concern that the social ends to which technologies were directed may be driven by private rather than public interests. A further concern was whether commercial funding of this area would lead to therapies just for the few rather than the many. As noted earlier, there was a strong conditionality around the acceptance and purposes of stem cell research.

There was seen to be an inherent tension, also picked up in certain stakeholder groups, as to whether commercial concerns would be sensitive to these issues or whether, in the rush to the market, commercial, scientific and regulatory forces would combine to push stem cells technologies in increasingly controversial ways. There was a concern around a paradox of discovery, in that a significant push for commercial applications may ultimately impede progress of the field by investing in the wrong areas.

In addition to these substantive concerns around the ends to which stem cell technologies were directed, there were also a number of more procedural concerns with private sector interests in this area. These included issues such as openness and the disclosure of information, particularly around clinical trial data; breach of consent around how embryonic stem cell lines were used; trust in commercial organisations to uphold public concerns; and a fundamental difference in the way in which science is done and communicated, predicated around protecting intellectual property and manageing risks in the private sector, and sharing knowledge and discussing uncertainties surrounding the science in the public sphere.

This latter issue is important. To an extent, public trust in this area is a corollary of the fact that the vast majority of the science and clinical practice in this area is undertaken by academic scientists. **Academic scientists were viewed to represent certain values: openness, honesty and working for the public good.**

A challenge is how leadership of those values is maintained in the move towards commercialisation. This is a particular issue given the strong translation focus associated with research funding and the science and innovation framework in the UK. This 'mode 2' model of research moves away from investigator-initiated and discipline-based knowledge production, to one which is context-driven and focused on closer working between science and various other, particularly commercial interests.

Conversely, from the perspective of commercial stakeholders, innovations in the academic field were felt to be controversial and pushing social boundaries in a way that was potentially unhelpful. Given the long lead times and significant investment needed, there were concerns that such developments may be mediated through the market and impact on investor confidence – as has recently happened with controversies in the pharmaceutical sector. More broadly, other stakeholders have noted that systems for the development of regenerative applications do not fit the traditional blockbuster model of innovation in the sector.

These issues aside, a large number of stakeholders highlighted that there was an **investment gap in the space between basic research and clinical applications,** which would require the cooperation and cooperation of research councils, the NHS, medical research charities and industrial partners to address. The need for this first stage capital was a significant blocker to progress in the field.

In this regard, it was recognised by workshop participants that commercial and public interests were not necessarily in conflict. There are also positive outcomes to be gained from working in a mode 2 model of research – for instance it was highlighted that there were opportunities for greater patient involvement in shaping the ends to which medical technologies were directed. It was also noted that this discussion could be opened up to other interests.

Public investment and the affordability of therapies was the final concern to be highlighted in this area, particularly in terms of uptake through the NHS. The public were keen not to divert resources from an already overstretched health service and it was noted that universal access to successful applications would be very expensive. There were also concerns around opportunity costs of investment, the diversion of investment from lower profile treatments and the medicalisation of the societal issues associated with ageing.

However**, it was recognized that the NHS provided an important platform on which to trial new clinical applications and the regulatory frameworks in the UK meant that products had high clinical and ethical standards**. Moreover, as a significant proportion of NHS spend was on palliative care and support around diseases of ageing and degenerative conditions, there would be

substantial cost savings. NHS pull would act as a considerable force to attract investment and there was viewed to be a genuine opportunity for public-private partnerships focused on clinical ends.

Given funding constraints, one final issue that emerged was the **potential for medical research charities to form a rainbow coalition and develop a collective campaign for stem cell research**. This was not only thought to have the potential to raise a substantial sum of money, but also to help facilitate public awareness and engagement in this issue more generally, as well as driving it higher up the political agenda.

4.4 Governance

The governance of UK stem cells was often viewed as a success story by participants. Most strongly articulated by government stakeholders, who saw the UK as leading the world in this area, **many viewed the supportive regulatory environment as a significant factor in contributing to favourable public opinion and assisting development of research**.

However, governance in this area is complex and often contested. When exploring governance, a distinction can be made between the systemic and institutional control of science through government and regulators (the hard infrastructure governance – explored next); to that of the social relations, informal networks and professional cultures which also act to shape the field (the soft infrastructure – explored in section 4.5 below).

In terms of the hard infrastructure of governance, there was **tension highlighted between a permissive legislative framework and the very tight regulatory systems in operation in the UK**. Certain stakeholders noted that the licensing applications to work on ES cells in particular were cumbersome and time-consuming – potentially acting as acting as a brake on innovation. It is notable that regulators saw one of their key roles as helping to assist commercialisation in this area - and were mindful of regulatory streamlining to attract more inward investment.

This notwithstanding, robust regulation was seen to provide a significant competitive advantage to the UK, including developing trust in the provenance and safety of stem cell lines; high ethical standards with regard to informed consent; and robust procedures governing the use of ES cells. All these were seen, in various ways, as helping to facilitate the conditional support of stem cell research in the UK and help set it apart from other countries working in this area.

Much has been made of the future-proofing of regulations in the UK, with the new Human Fertilisation and Embryology Act seen as an exemplar. However, the fragmentation of regulation in the UK between HFEA, HTA, GTAC, MHRA and the

EMEA was seen as an issue in the development of stem cell therapies, further complicated by issues at the EU level through the EMEA. How the science shapes up, and whether products are viewed as therapies or medical devices was uncertain for many stakeholders. Standards covering good manufacturing practice regulation in clinical-grade stem cell lines were also an issue. Moreover, the science is also beginning to shape some of the categories covering various aspects of regulation – around the relationship between the regulation of embryos and IPS cells, for instance: what an IPS cell is; what the ethics governing it are; who should be the competent and relevant authorities, and so on.

A wider issue concerned the need for informed consent for the use donated embryos. As noted earlier, given the possible future uses of stem cell lines, it may be difficult to predict what constitutes a serious disease when consent is gained. Moreover, as it is precisely when stem cells are developed into a stem cell line that they become productive in an innovation sense, international access and global use means it may be difficult to control how such stem cells are used. Given that the public were keen to provide donors with a significant amount of information around the use and control of donated embryos, the governance of this process is important.

It may be that, given these difficulties, only consent to general use can be gained, and that oversight bodies governing stem cell banks also have lay public, donor and patient representatives. This will help ensure that a situational ethics that takes account of public values is in place to help govern usage. This issue is important as stem cell banks were not only viewed as a resource to lead innovation but also a means to lead ethical debates in this area; public trust was central to this.

The final issue of governance was in relation to clinical trials - specifically risk-taking in relation to experimental therapies where the existing treatment is poor. Certain stakeholders noted that the UK has a zero risk system, and certainly members of the public highlighted the need to take the individual and patient perspective into account much more effectively. This presents a challenge to the current paternalistic model governing clinical trials and in particular the information provided to patients in these circumstances. It may be that lessons can be learned with regard to how novel HIV drugs were tested in the US, being driven strongly by patient groups through expanded access programmes.

4.5 Science and the public: the role of future dialogue

The final conclusion relates to wider relationship between science and the public. It refers to the soft infrastructure of governance noted earlier - the social relations, informal networks and professional cultures which also act to shape and control the field.

Public dialogue in this regard should not be seen as a set of one-off discussions to secure a licence to operate – it is about asking what sort of debates and under what conditions stem cell research should be encouraged to advance.

In this regard, openness, engagement and science communication are a crucial part of governance. Both members of the public and a variety of stakeholders noted the importance of dialogue to the development of trust in stem cell science.

As noted earlier, there were differences in conversations of scientists and clinicians between the interviews and the workshop. Whilst the role of ethics and society was recognised in the interviews, it was not dominant. Rather, this 'professional narrative' was much more focused on the current state of the science, the need for investment in basic research and the risks in clinical practice. It will be important that there is two-way learning between public and private conversations. It will be important to highlight uncertainties publicly, and reflect back on social views privately**. In short, dialogue needs to permeate research culture – rather than being seen as done by special people in special places.**

So what does good dialogue look like going forward? Whilst formal exercises such as this research undoubtedly have a role to play, running another big event on cord blood or IPS cells is perhaps not the most crucial issue. Rather it will be further imbuing the professional culture and practices of stem cell research with the spirit of open discussion. The UK has done this well to date, but given the high levels of public support there is a risk of complacency. Also, as noted earlier, the biggest challenge to this area will be the tension between public and private interests as there is a move to commercialise academic research. The issue is one of cultures and practices – this needs to continue and be enhanced.

Finally, the responsibilities of funders are important in this regard. The role of research councils is shifting as the role of research shifts, from a focus on grant administration to taking a much more active role in the shaping of technologies in society. There have been major strides in this area recently – not least in the form of science in society programmes with the research councils and a general trend towards greater lay involvement in policy making.

Whilst many of the issues that have been raised through the dialogue fall outside the core scope of research councils, there is an opportunity to work with institutions in the public and private sectors to help ensure messages are taken forward. Moreover, there is also the opportunity to build on foundations and work with individual scientists - through programmes, training and support – to help create an institutional culture of research that places public value at the heart of research decision making.

Overall conclusions and recommendations

1. There was conditional support for funding all avenues of stem cell research. A focus on basic and translational research should be priorities. For clinical research, priority should be given to serious diseases or injuries for which the current treatments are limited.

2. Key concerns expressed during the dialogue focused on whether research using embryonic stem cells is necessary and how 'serious' disease is defined. These issues are likely to evolve in the future, making it difficult to establish firm guidelines on stem cell uses and donor consent. Ethics committees will need to account for donor and public views as the science develops.

3. There were significant health and wealth opportunities to be gained from stem cell research. There needs to be greater investment and coordination between public (research councils and NHS) and private (pharmaceutical and venture capital) sectors to achieve this goal. There is a significant opportunity for a coordinated campaign by medical research charities to raise the resources and profile of stem cell science.

4. The involvement of the private sector raised concerns about the means and the ends of research. For public trust to be maintained, therapies should reflect public rather than solely commercial interests, with a focus on serious diseases affecting society. Moreover, the need to protect and exploit intellectual property rights needs to be balanced with the need to disclose information in the public interest. Research councils and universities should account for these factors when commercialising research.

5. Whilst legislation in the UK was supported, tight regulation and the number of relevant authorities were viewed as cumbersome by a range of groups, including researchers, clinicians and the public. There needs to be coordination between regulators to ensure the seamless transition of research into routine clinical practice, which takes account of the novel aspects of cell based therapies.

6. The governance of clinical trials was viewed as risk adverse by certain research and commercial respondents. Providing there was informed consent and potential risks had been fully explained, there was public support in trialling experimental therapies with patients. The views of patients should be paramount when making decisions around the development of stem cell therapies.

7. Future dialogue should focus on the cultures and practices of research within institutions. Whilst large structured dialogue events are important,

it will be fundamental that the everyday practice and discussion of science is mindful of societal views. Uncertainties in stem cell science should be communicated openly if the public debate is to avoid being dominated by hype. Substantive areas of interest include the private banking of cord blood and the potential of induce pluripotent stem (IPS) cells.

Glossary

Adult stem cells (AS cells): are undifferentiated cells found throughout the body after embryonic development. They can self renew and differentiate to yield the major specialized cells of the tissue or organ type in which they are found. Their job is to replace and replenish cells that are continually lost by depletion and damage. They are multipotent, able to form a limited number of cell types. They are used therapeutically for a number of treatments including bone marrow transplants and skin grafts.

Blastocyst: is the structure formed in early embryo development, 5-7 days after fertilisation. It consists of an inner cell mass, which will form the embryo and ultimately all adult tissues and organs; and an outer cell mass, which forms the placenta. Embryonic stem cells are harvested from the inner cell mass.

Cytoplasmic hybrids: involves the creation of an embryo through the insertion of human nuclear material into an enucleated animal egg, typically a cow or rabbit egg.

Embryonic stem cells (ES cells): are derived from the inner cell mass of an early stage embryo. They are pluripotent – having the ability to differentiate into all of the tissue types in the adult body. They can also self renew. To date, there are no therapeutic treatments from embryonic stem cell research.

Induced pluripotent stem cells (IPS cells): are adult somatic cells that have been modified, by inducing the expression of certain genes, to have the ability to differentiate into all of the tissue types in the adult body. They hence have the potential functionality of embryonic stem cells.

Human Fertilization and Embryology Authority (HFEA): is the UK's independent regulator overseeing the use of gametes and embryos in fertility treatment and research.

Human Tissue Authority (HTA): regulates the removal, storage, use and disposal of human bodies, organs and tissue from the living and deceased.

Medicines and Healthcare products Regulatory Agency (MHRA): is the government agency responsible for ensuring that medicines and medical devices work, and are acceptably safe.

Somatic cell nuclear transfer (SCNT): involves removing the nucleus from an egg and inserting donor DNA into this 'empty' egg. The egg-cell combination is then stimulated to develop into a blastocyst, from which embryonic stem cells can be extracted. The aim of carrying out this procedure is to obtain stem cells that

are genetically matched to the donor. Presently, no human stem cell lines have been derived from SCNT research.

Tissue-specific stem cells (TS cells): is a generic term to refer to stem cells that can be sourced from body tissues – including adult stem cells, those derived from cord blood and those derived from foetal material. Such stem cells are multipotent and can only differentiate into their own or a related cell type.

5 Appendix 1: Methodology

5.1.1 Phase 1: Project scoping

A scoping meeting was held with the Stem Cells Oversight Group (OG) on 12th October 2007 to determine the overall goals of the project, the scope of the issues to be covered and the timetable for milestones and deliverables.

The following was agreed:

- Three workshops to be held in five areas focusing on the visions, sources and applications of stem cells;
- Funding and the international context to be incorporated as topic areas;
- The strengths and limitations of embryonic and adult stem cells to be reviewed in parallel;
- OG to provide a list of experts for the project;
- Clinicians to be represented in the study.

Omnibus survey and media launch

Public attitudes towards stem cell research were explored through an omnibus survey, comprising a nationally representative panel of 1013 people aged 16+. Results from the survey (see appendix 2) were used to help launch the project at a press event at the Science Media Centre on 26th November 2007.

5.1.2 Stage 2: Recruitment

Recruitment for the stakeholder interviews and the workshops was undertaken by BMRB's in-house qualitative recruitment team.

Stakeholder interviews

Stakeholders were identified by the BMRB research team in conduction with the OG. Nine stakeholder groups were identified of interest to the study and interview quotas set. The following recruitment procedures were then undertaken.

- A letter was sent on the behalf of BBSRC and MRC notifying the stakeholder of the project and its aims;
- A phone call was made by BMRB field team following and an appointment made.

The following sample was achieved:

Table 2: List of stakeholder groups interviewed during the research

Stakeholder group	Number of interviews
Research scientists	12
Clinicians	6
Social scientists/ ethicists	5
Commercial and pharmaceutical	4
Religious	5
Medical charities	5
Pro life groups	4
Funders	3
Government and regulators	5

Workshop recruitment

A quota sample to recruit 200 respondents was developed, stratified across five workshops, each comprising 40 members of the public. Quotas were set for age, socio-economic status and ethnicity, reflecting the demographic profile of the local area. Attitudes to stem cells were screened to ensure the sample broadly matched public attitudes, as profiled in the results of the BMRB omnibus survey.

Table 3: Achieved sample for the workshop:

Region (Venue)	Gender	Social grade	Ethnicity	Total Number
London W1	M 19 F 22	ABC1 24 C2DE 17	White 27 Black 7 Asian 7	41
W2	M 17 F 22	ABC1 23 C2DE 16	White 25 Black 7 Asian 7	39
W3	M 15 F 21	ABC1 21 C2DE 15	White 24 Black 6	36

			Asian 6	
Bristol				
W1	M 18 F 20	ABC1 19 C2DE 19	White 35 Black 1 Asian 2	38
W2	M 18 F 20	ABC1 19 C2DE 19	White 35 Black 1 Asian 2	38
W3	M 18 F 19	ABC1 18 C2DE 19	White 34 Black 1 Asian 2	37
Cardiff				
W1	M 20 F 20	ABC1 23 C2DE 17	White 36 Black 3 Asian 1	40
W2	M 18 F 18	ABC1 22 C2DE 14	White 32 Black 2 Asian 1 Other 1	36
W3	M 17 F 17	ABC1 22 C2DE 12	White 30 Black 2 Asian 1 Other 1	34
Newcastle				
W1	M 20 F 22	ABC1 20 C2DE 22	White 37 Black 0 Asian 5	42
W2	M 16 F 20	ABC1 19 C2DE 17	White 31 Black 0 Asian 5	36
W3	M 16 F 20	ABC1 19 C2DE 17	White 31 Black 0 Asian 5	36
Edinburgh				
W1	M 17 F 22	ABC1 18 C2DE 21	White 33 Black 0 Asian 6	39
W2	M 18 F 21	ABC1 19 C2DE 20	White 34 Black 0 Asian 5	39
W3	M 17 F 21	ABC1 18 C2DE 20	White 34 Black 0 Asian 4	38

Public participants received incentive payments of £70 for workshops one and two, and £75 for the third workshop.

A scientist and a social scientist/ethicist were also recruited for each of the workshops. Their role in the dialogue process was twofold: firstly, to provide information that would assist in the deliberation of public participants; secondly to engage in the deliberative process, listen to the public and contribute to discussions.

The following recruitment procedures were undertaken:

- An email was sent inviting the specialist to the workshop;
- A telephone call was made, discussing the workshop focus and the role of the specialist in more depth;
- A confirmation email was sent, highlighting venue and logistical arrangements, as well as recapping on key issues that had emerged during the briefing.

The following specialists attended the workshops:

Table 4: Scientists and ethicists in the workshop

Area	Workshop 1	Workshop 2	Workshop 3
London	Stephen Minger (King's College London) Amanda Dickins (King's College London)	Robin Lovell-Badge (National Institute for Medical Research) David Jones (St Mary's University College London)	Chris Mason (University College London) Steven Wainwright (King's College London)
Bristol	Melanie Welham (University of Bath) Susan Weber (University of Exeter)	Melanie Welham (University of Bath) Christine Hauskeller (University of Exeter)	Neil Hanley (University of Southampton) Ann Bruce (University of Edinburgh)
Cardiff	Charlie Archer (Cardiff University) Jennie Gunning (Cardiff University)	Anthony Hollander (Bristol University) Neil Stephens (Cardiff University)	Nazar Amso (Cardiff University) Derek Morgan (Cardiff University)
Newcastle	Michael Whitaker (Newcastle University) Dana Wilson-Krovacs (University of Exeter)	Jon Frampton (University of Birmingham) Donald Bruce (Society, Religion and Technology Project)	Jaap van Laar (Newcastle University) Jan Deckers (Newcastle University)
Edinburgh	Tilo Kunath (University of Edinburgh) Nicola Marks (University of Edinburgh)	Neville Cobbe (University of Edinburgh) Sarah Cunningham Burley (University of Edinburgh)	Dr Brendan Noble (University of Edinburgh) Dr Calum McKellar (Scottish Council on Human Bioethics)

5.1.3 Stage 3: Stakeholder interviews

Forty nine telephone interviews were conducted between January and October 2008.

The interviews had two main aims:

- to provide a systematic analysis of how different stakeholders view the direction, pace and vision for stem cell science and the related social and ethical issues;
- to inform the development of the workshops, particularly the areas of focus within the discussion guide and the stimulus material used to inform debate.

The interviews lasted approximately 40 minutes, were digitally recorded and transcribed for analysis. The following issues were covered:

- Vision for biomedical and stem cell science;
- Research and social issues related to ES cells;
- Research and social issues related to TS cells;
- Research and social issues related to therapies.

A full topic guide is given in appendix 3.

5.1.4 Stage 4: Workshops

Participants were reconvened for three deliberative workshops lasting from 10.30am to 4pm at following locations and dates:

Table 5: Workshop locations and dates

Area	Workshop 1	Workshop 2	Workshop 3
London	5 April 2008	26 April 2008	24 May 2008
Bristol	12 April 2008	3 May 2008	31 May 2008
Cardiff	12 April 2008	3 May 2008	31 May 2008
Newcastle	12 April 2008	10 May 2008	7 June 2008
Edinburgh	5 April 2008	10 May 2008	7 June 2008

The workshops were divided into whole group sessions, which comprised plenary discussions, presentations from experts, and voting sessions using electronic IML audience engagement technology; and small group sessions, in which the issues were discussed in depth and audio recorded for analytical purposes. A lead moderator directed the workshop overall and each small group was conducted by a co-moderator. Discussion followed a detailed topic guide (see appendix 3), summarised as follows:

Workshop 1

- aspirations and concerns for medical science and stem cells, including discussion of the social and economic drivers shaping research in the future;
- understanding and views on stem cells science and ethics, including regulatory and commercial issues;
- discussion of four competing visions for stem cell development derived from stakeholder interview data, including perspectives from scientists, social scientists, campaign groups, and industry.

Workshop 2

- Views on the benefits, clinical uses, limitations and overall public value of TS cell research, specifically adult stem cells, cord blood and foetal tissue;
- Views on the benefits, clinical uses, limitations and overall public value of ES cell research, specifically IVF, SCNT, hybrids, and IPS cells.

Workshop 3

- Views on the research and clinical value of stem cell banks, including issues of donation and governance;
- the research and therapeutic uses of stem cells, including basic research, the treatment of serious diseases, and as tools for understanding disease and testing drugs;
- Patient safety and clinical trials, particularly the diseases that participants felt should be prioritised for research;
- Final reflections on the workshops overall and feedback messages to BBSRC and MRC.

5.1.5 Stage 5: Q methodology

Q methodology is an approach to studying human subjectivity. It involves individuals sorting a set of statements or images associated with the topic under investigation, the results of which are then subjected to statistical analysis. Although it employs statistical data analysis techniques it is designed for use with relatively small numbers of individuals.

For this study a concourse of nearly 250 statements was compiled from a wide range of publicly available sources that included parliamentary and regulatory reports, industry and interest group documents, press reports and various online sources. From this a set of 46 statements was derived, designed to represent all of the main categories of statement contained in the concourse. The statements were randomised and printed onto cards. A set of Q-sort materials, including the set of statements, a data recording sheet and a set of written instructions was sent to all workshop participants in June 2008, a few weeks after the final series of workshops.[4]

Participants were instructed to begin by sorting the cards into three piles: those with which they agree, those with which they disagree, and those about which they are uncertain or do not have a view. Statements were then further sorted according to relative strength of agreement or disagreement on a scale that roughly approximates a normal distribution pattern. When the sort was completed the number of each card was marked onto a data recording sheet that replicates the prescribed pattern into which the cards were sorted.

A total of 65 responses was received, a response rate of 36% (based on a sample of 181 from the final workshop). Of these, 15 were incomplete or spoiled, resulting in a sample of 50 valid Q-sorts for analysis, which represented 28% of all workshop participants. These Q-sorts were fairly evenly distributed across the five workshop locations, with a mean of 10 sorts from each location (range 9-11). 68% of the final sample was female and 32% male.

Q sort materials were also sent out to the scientists and stakeholders whom we had interviewed during the first phase of the study. The purpose of this was to provide data on expert viewpoints that could provide a comparison with those of the members of the lay public who had participated in the workshops. Only six of the experts returned a completed Q sort: four scientific researchers and two individuals concerned with the ethical and social aspects of stem cell science. Despite the small number returned this sample proved sufficient, as shown in the results section below, to provide useful indicators for the purpose of comparison with the participant data set.

[4] A list of the statements and a copy of the data recording sheet, which illustrates the pattern into which the cards were sorted, are given in the appendices.

The numerical data generated by each Q sort (the pattern of card numbers entered on the data recording sheet) was input to a data file. The data was then subjected to factor analysis (Principal Components Analysis) using PQMethod software. The factors identified by this process represent different points of view. Unlike most applications of factor analysis, rather than clustering variables Q methodology uses the technique to cluster individuals according to the degree of correlation between their rankings of the Q sort statements. The factor analysis identifies those individuals whose points of view correspond most closely with that represented by each factor. It also enables the researcher to reconstruct an ideal-typical Q sort for each factor, on the basis of the factor score for each statement. These ideal-typical Q sorts provide the basis for interpreting the meaning of each factor. Each factor can be characterised by a careful reading and interpretation of the combination of statements, with particular attention to those that receive high positive and negative scores. Some of these statements may receive similar scores on more than one factor; the analysis therefore attends also to those that are scored significantly differently for a given factor than for any other factor (these are referred to as 'distinguishing statements').

For the purpose of this study the factor analysis was carried out in two stages. In the first stage the data collected from each regional group of participants was factor analysed separately, resulting in five sets of results. In addition to this the set of 'expert' data was also factor analysed. In each of these analyses either one or two distinct factors or viewpoints were identified. The factor output from these six analyses, in the form of the ideal-typical Q sorts representing the broad viewpoint expressed by each factor, were then used as input to a second-order factor analysis. This technique first enables any distinctive differences within the various regional subgroups to emerge, rather than being 'lost' in a larger aggregated data set. It also enables the researcher to get some indication of the distribution of a viewpoint, despite the small numbers involved, by looking at the extent to which it recurs in different subsets of the data. Findings are in Appendix 4.

5.1.6 Phase 6: Analysis and reporting

All of the workshop sessions were digitally recorded and audio transcribed. The transcripts were then analysed through a technique called Matrix-Mapping. Based on the topic guide, the researchers' experience of conducting workshops and a preliminary review of the data, a thematic matrix was constructed and the transcript material was then summarised into this framework.

BMRB then reviewed the material and identified features within the data: defining concepts, mapping the range and nature of phenomenon, creating typologies, finding associations, and providing explanations. This approach identified themes that emerged from the workshops, as well as highlighting differences between different groups. Key issues and underpinning features were then used to

construct the reports. Verbatim quotes were also used to illustrate and illuminate the findings.

Workshops from each wave were charted onto the matrix until researchers identified a saturation point after which no new theoretical insights were emerging. On reaching this stage, the remaining transcripts were used to check for anomalies, differences and to substantiate the analysis developed. Given the complexity and wide-ranging nature of the issues covered in the workshops, as well as the relative fluidity of the workshop form of discourse for data collection, it was found necessary to chart in their entirety over 30 of the total 60 workshops conducted before reaching saturation point.

Data collected from IML voting and Q methodology was used as a quantitative means of mapping and substantiating the themes emerging through matrix analysis of workshops.

Analysis of expert and stakeholder interviews was conducted in tandem with workshop analysis. These were analysed in most cases by the researcher who had carried out the fieldwork. A framework based upon the topic guide was drawn up as the basis for descriptive summaries of each interview. Interviews were then clustered using the initial recruitment groupings by professional interest to lift the data into an analytical frame, seeking conceptual patterns and themes emerging within each cluster.

6 Appendix 2: Results from the omnibus survey

Q1: What comes to mind, if anything, when I say the phrase 'stem cell research'?

	%
Medical treatments/ treating disease	23
GM/ Cloning	12
Science/ technology	6
Embryos for research	5
Cancer research	3
Babies	3
Good idea	2
Medical research	2
Nothing	29
Don't know	1
Others (all ≤1%)	14

Q2: Are you very, fairly, not very or not at all familiar with stem cell research?

	%	%
Very familiar	6	49
Fairly familiar	43	
Not very familiar	29	51
Not familiar at all	22	
Don't know	*	*

- 49% awareness - 6% increase since Eurobaromter survey in 2005
- 35% awareness 16-34 age group - higher awareness 35+ age group
- Higher awareness – AB social group (61%) compared C2 DE (both 41%)

- No significant difference - gender

Q3: Overall, which of the following best captures your view about research using embryonic stem cells?

	%	%
Approve usual	47	73
Approve tighter	26	
Not approve except under special circumstance	17	23
Not approve under any circumstances	6	
Don't know	4	4

- 73% approval - 11% increase since EB 2005 - *main shift from DK*
- 60% approval 16-24 age group; 67% 65+ compared to 80% approval 45-54
- ABC1 78% approval; C2 DE 68%
- Male 77% - female 67% approval

Q4: Suppose scientists were able to get all the stem cells they needed for research without having to get them from embryos. Which of the following would best capture your view?

	%	%
Approve usual	48	76
Approve tighter	28	
Not approve except special	15	20
Not approve under any	5	
Don't know	4	4

- 76% approval - 7% increase since EB 2005 - *main shift from DK*

- 69% approval 16-24 age group; 70% 65+ compared to approval 89% 45-54; 81% 55-64.

- ABC1 82% approval; C2 DE 72%

- Male 80% - female 72% approval

7 Appendix 3: topic guides

Workshop 1

Time	Session and aims	Topic areas	Tools/Stimulus material
10.30 Whole group	*Session 1: Welcome and introduction* Introduce study aims Canvass individual views in general on science and stem cells (for tracking)	Overview of study Welcome from Research Council Representative Housekeeping and ground rules; mention evaluators Warm up questions, attitudes to S&T; General questions on stem cell research, including awareness and attitudes	IML interactive voting
10.50 4 Small Groups	*Session 2: My vision for medical science* Warm up group Understand peoples unprompted aspirations for medical science and stem cells	Reiterate ground rules Introduce participants to one another Ice breaker: what comes to mind when say the word scientist What are our aspirations and concerns for medical science? Knowledge of stem cells previously? [link back to session 1] Do people have any particular aspirations and concerns about stem cells? Discussion of societal changes that will happen over the next few decades. How do these trends affect their views?	Handouts on social trend analysis by Henley **(See Annex 2)**
11.50 Whole group	*Session 3: Introduction to stem cell research* Provide people with a broad understanding of stem cell	What is stem cell research What are its potential applications and challenges What are the ethical issues How does the UK regulate research / comparison to other countries	Presentation by a scientist and social scientist

	development in UK	What is the UK investment in stem cell/ wider innovation and commercial issues Q&A	
12.10 Small groups	*Session 4: Group discussion of presentation* Enable people discuss and get up to speed with stem cell research and development in the UK	Understanding of and questions about: • What stem cells are • Stem cell sources • Research and applications • Research challenges • Embryo research ethics and regulation • Funding and commercial issues	Pictorial handouts summarising key issues Scientist and social scientist as a resource for the group **(See annex 3)**
12.50pm	Lunch		
1.30pm Small groups	*Session 5: Different visions for stem cell science* Explore four different visions for stem cell science Explore views on opportunities to influence science trajectories	Taking each in turn (15 mins each): Does the vision resonate with their own views What do people think is good about this vision What are the problems or concerns with this vision If you could influence this persons visions, what would you say to them Potential probes V1: Hype; commercialisation; UK position in world; investment in NHS V2: Other things to fund with the cash; clinical risks; other world diseases – who benefits V3: Ethics of embryo research; necessity given research in adult stem cells; hype; responsibilities for public debate V4: Who benefits; the need to fund both areas; individual and clinical risks; individual decisions vs societal consequences.	Four handouts - each exploring different visions, aspirations and concerns for stem cell science (based on analysis of stakeholder interviews) **(See annex 4)** Discussion with scientists/ ethicist

		Overall reflecting on visions, their own discussions and social trends (30 mins): Who will benefit from stem cell research? Who do they feel is controlling research? Do they trust how the science is being developed? Do they feel stem cell research will be available and affordable? What will stem cell research mean for them and their family?	
2.45pm	Break		
3.00pm Small groups	*Session 6: Reflections on day* To understand which issues influenced views To understand information needs	What 3 things would you feed back to the MRC/BBSRC about today What has surprised you most about today? Have people change their minds a result of discussion? What key things influenced? What views have not changed and why? What information do they feel people need to make judgments on stem cells Probe: Benefits & risks? Current regulations and regulation enforcers? Who is responsible for moral limits? What processes & techniques used? Who are funders and beneficiaries?	
3.20pm Whole group	Session 7: Feedback, voting and thanks To review key thoughts from the day To track impact of	Feedback 3 top issues for the day from each group for BBSRC and MRC to consider Repeat voting on selected questions from session 1.	IML voting on key tracking questions **(See annex 5)**

	discussion on views To get feedback on how the day went To explain what happens next	Voting on feedback questions Voting on evaluation questions Thanks and next steps	
3.40pm	Ends		

Annex 1: IML Voting Questions

Q1: What gender are you?

- Male
- Female

Q2: What age group do you fall into?

- 16- 34
- 35-54
- 55+

Q3: Do you have any children in your household?

- Yes
- No

Q4: Do you regard yourself as religious?

- Yes
- No

I now want to ask you some statements people have said about science. For each, tell me how much you agree or disagree.

Q5-10: Britain needs to develop its science to enhance its international competitiveness

Scientists seem to be trying new things without stopping to think about the risks

We depend to much on science and not enough on faith

I trust scientists to tell the truth

The media sensationalises science

Science is driven by business – at the end of the day it is all about money

- Agree strongly
- Agree
- Neither agree nor disagree
- Disagree
- Disagree strongly
- Don't know

Q13: How familiar are you with stem cell research?

- Very familiar
- Fairly familiar
- Not very familiar
- Not at all familiar

Which of the following statements are true?

Q14: Stem cells are unspecialised cells that have the ability to renew themselves (TRUE)

Flash up: Stem cells are immature cells that have not yet developed into the specialised cells that make up our organs and tissues. And they have the ability to renew (make identical copies of) themselves almost indefinitely.

Q15: Stem cells are only found in the brain and heart of adults (FALSE)

Flash up: They are found throughout the body and are present from just after fertilisation of an egg right through to adulthood.

Q16: Stem cells can only make brain and heart cells. (FALSE)

Flah up: Stem cells are able to generate into all cell types in the body.

Q17: One of the key sources of stem cells for medical research is human embryos (TRUE)

Flash up: Early stage embryos - usually about five days old - are used for embryonic stem cell research.

Q18: Which, if any, most closely describes your view about the use of human embryos for research?

- The use of human embryos for medical research is never acceptable
- I believe using human embryos for medical research is permissible to find treatments for serious diseases and fertility research, but not for other types of research
- The use of human embryos is always acceptable for all types of medical research
- I don't know

Q19: During 2005/2006, how much money was spent by the BBSRC and MRC on stem cell research?

- £5.8 Million
- £25.5 Million (correct answer)
- £55.1 Million
- £107.6 Million

Annex 2

Societal changes within the UK that may impact science and medical research in the next 10 -15 years

Ageing population and agelessness

We are living in an increasingly ageing society due to medical advancements and greater focus on wellbeing. As older people are more susceptible to health problems, this could have huge impacts on our society.

4. At present there are more people aged over 60 than under 16. By 2025 there will be more people over 60 than under 25

5. In 1981 life expectancy was 76 years for men and 81 years for women. By 2026 this is expected to rise to 84 and 87 respectively

As older people increasingly live youthful and active lifestyles, societal perceptions of 'being old' are changing. This means that people will be expecting to maintain good health for longer.

Rising prevalence of degenerative diseases

The prevalence of degenerative diseases such as Parkinson's disease is rising in the UK.

2. 700,000 people in Britain have dementia of which 417,000 have Alzheimer's disease. The number of Alzheimer's sufferers is predicted to increase to 1.7m by 2050

3. Dementia costs the UK £17bn a year of which £11bn is due to Alzheimer's. An increase in 1 million sufferers could double the cost

4. Approximately 1 in 500 people in the UK have Parkinson's disease. Of the 10,000 people diagnosed each year, 1 in 20 will be aged under 40

In an ageing society an increase in degenerative diseases will create added demand on health services.

Societal changes within the UK that may impact science and medical research in the next 10 -15 years

Widening income and health inequalities

Although people in the UK are now financially better off than in the past, the gap between rich and poor remains high compared with other wealthy nations. This combined with the increasing expense of healthcare may create a divide within society where some can afford their own private medical care and others can not.

Exclusive health services such as cord blood and stem cell storage companies now exist. People are willing to pay for these services in hope that they can be used in the future. In order to prevent a scenario where medical treatments are only available to the wealthy, large scale Government involvement and investment from the NHS will be required to ensure that as many people as possible have access to potential life changing health treatments.

Government and personal spending on health

With limited resources the Government is required to make careful decisions regarding budgets. However, rising demands on the health service and increasing costs of the NHS are further tightening budgets and so health programmes need to be assessed on their potential contribution to society.

Over the last decade the NHS drugs bill has soared from £4bn to £8.2bn a year and is set to continue to rise

International funding for health projects has been reduced as European Commission budgets were cut from
$1.25bn to $0.47bn between 2007 and 2013

Heart Bypass Cost:

UK: £15,000
France: £13,000
US: £13,250
India: £4,300

There is rising expenditure on health by households - according to ONS data, the average UK household has spent 2% of all expenditure per year since 2001. In 1991, the amount was only 1%

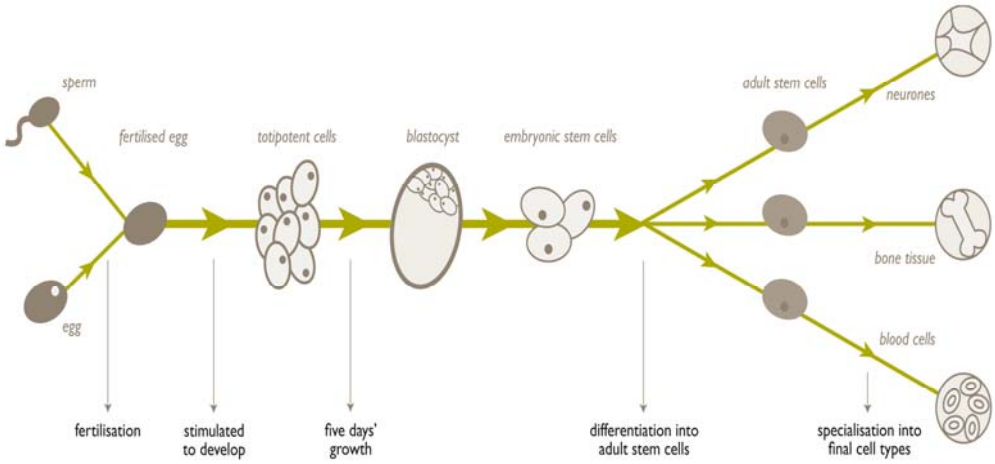
Medical tourism is on the increase. In 2005, approximately half a million foreign patients travelled to India for medical care, whereas in 2002, the number was only 150,000.

Annex 3

Handout 1

What is stem cell research?

Stem cells are immature cells that have not yet developed into the specialised cells that make up our organs and tissues. They are found throughout the body and are present from just after fertilisation of an egg right through adulthood. Unlike specialised cells, stem cells are able to generate many different types of cells, such as the beating cells of the heart or the insulin producing cells of the pancreas. And they have the ability to renew (make identical copies of) themselves almost indefinitely.



There are two different types of stem cells:

Embryonic stem cells: come from embryos that are about five days old – when the embryo is a ball of about 50-100 cells. This type of cell can give rise to all cell types in the body. The most common source of these cells is from embryos left over from IVF treatments. These are only used if the couple has given their consent. Scientists are also looking at other ways to create embryos for research. We will be exploring this more in the next workshop.

Adult stem cells: Adult stem cells are found in many parts of the body, such as the eye, the bone marrow, muscle and the brain. Their job is to replace and replenish cells that are continually lost by depletion and damage. The term adult stem cells can be misleading. They are found in babies, children and adults, and even in the umbilical cord blood. Unlike embryonic cells, they can naturally only give rise to a limited number of cells. Scientists are looking at how adult stem cells can be reprogrammed to produce more cell types.

Handout 2

What are its potential applications?

Many diseases are caused by the premature death or malfunction of cells. For instance, Parkinson's disease is due to brain cells dying, while type 1 diabetes is caused by faulty pancreatic cells. Scientists believe that stem cell therapy may offer a revolutionary way to treat such conditions by repairing diseased body tissues and replacing them with healthy new cells. Other potential applications include: brain diseases such as Parkinson's; central nervous system injuries and diseases such as multiple sclerosis; blood disorders such as sickle cell and leukaemia. Stem cells can also help us to understand new treatments for cancers. They can also be used for drug development. We will be looking in depth at applications in workshop 3.

What are the challenges associated with stem cell research?

Researchers do not yet understand exactly how stem cells work. To be able to release their potential, they first must learn how to direct stem cells to become, for example, muscle cells for damaged hearts or neurones to treat brain diseases. Scientists also have to learn how to make sure that stem cells do not multiply in an uncontrollable way and create tumours.

Handout 3

What are some of the Ethical issues?

Some people think that embryos, no matter how early, represent human life and that it is wrong to use them for research or medical purposes. Others, however, do not believe five day embryos -which are no bigger than a grain of sand- are fully human, and believe that the potential of embryonic stem cells to cure many deliberating and devastating diseases outweigh any ethical concerns about using them.

How does the UK regulate research and how this compares to other countries?

In the UK, embryonic stem cell research is regulated under the Human Fertilisation and Embryology Authority Act (1990). Only research to find cures for serious diseases or fertility research is permitted, and embryos can only be used up to 14 days old. The creation of embryos for research is also permitted in the UK

Globally there are variations in the regulation of embryonic stem cell research. Countries such as Canada and Sweden have similar regulations to the UK - as does China though its systems for enforcement are less well developed. Embryonic stem cell research is more restricted in Italy, Germany, Poland and Portugal. The USA has no federal guidelines - some states ban it, while other state governments actively encourage it. Countries such as South Korea have much more permissive regulations.

Handout 4

What is the UK investment in stem cell research and what are the commercial issues?

BBSRC and MRC funding for stem cells in 2005-2006 was £25.5 Million. There are a number of wider commercial issues that impact on the development of stem cell treatments including how we develop intellectual property rights from scientific advances, lack of venture capital investment in the UK, the need to fund the translation of basic research to clinical applications, and issues over the uptake of medical technologies into the NHS.

Annex 4: Visions for stem cells

Vision 1: An industry vision

Dave Morris

Head of Venture Capital

Stem Cells UK plc

'Obviously we are at the cutting edge in terms of the science from a UK perspective, but where we often lose out is in terms of being able to build companies or commercialise the science into products that will actually reach patients.

You know, once you get this very clear breakthrough, whatever it might be, once people can see a clear benefit and therefore begin to think less about the risks, I think the issues around stem cells will change a lot. Because the minute that somebody gets off the bed and walks having had some sort of stem cell therapy into some spinal cord injury, this will go mad, you know, it will go wild.

Competing internationally is going to be hard. Take the Americans. Sure, there is not a lot of Federal money going into embryonic stem cell research, but when you then look at State level, if you look at sort of funding that is going in California, I mean, the money that our Government has announced it is putting in is just a joke. Singapore and Korea – they aren't so good at the science – but when they want a piece of the pie, boy do they make sure they are going to get a piece of the pie. They pump inordinate amounts of money into trying to attract, you know, business and technology and academics. It is like the industrial revolution isn't it? This could be another wave in terms of genetic revolution.

So what so we need to do - well - we have got the excellent science. We need to get investment. We need vibrant small stem cell companies. We need a public that is very supportive of the work that is happening and clearly understands why it is being done and what the benefits are, and also understands the risks. We need big pharmaceutical companies being a lead player in these new technologies. We need a good regulatory pathway so that we have worked out how we are going to trial them in patients and get people onto them effectively in this country. And we have also got to get the NHS to modernise and a take up some of these new innovative therapies. Because quite frankly, if the Department of Health isn't going to buy any of this stuff, why bother, you know?'

Vision 2: A vision from a social scientist

Dr Benjamin Hewitson

Senior Lecturer in Social Sciences

University of Ealing

'I think stem cell science will play a part in addressing some of these big societal challenges we are looking at. But, I mean, it's only a part. It's easy to get carried away with it. So an ageing society – you know, yes, we will be getting to stem cell therapies that help with things like dementia. But in reality it's going to be much more to do with social aspects of caring that will help people to look after an ageing society. If we put a tenth of the money going into stem cells into carers and community support – I think we would see a huge benefit.

In terms of stem cell treatments, I do think there will be breakthroughs. But if I am honest, if I'm a scientist and I'm working on stem cells, I'm actually uncertain about the impact of this work, and I'm even uncertain about it if I apply to you clinically as a patient.

So I think that government needs to think about putting in place, gradually over the next few years, a sort of biological public health safety net which can provide a degree of vigilance with respect to the monitoring of the application of stem cells. It's a bit like the sort of thing that's in place with drugs to manage side effects.

The difficulty and the difference is that whereas with drugs you can stop taking the pill and hopefully be okay, if there is a side effect, with stem cells, once they're implanted, if they start to become carcinogenic, then clearly that is a worry. You don't want to say, we're curing your Alzheimer's but we're giving you cancer, so there needs to be a thorough look at how that's going to be managed. You know, one of my real concerns is that in the rush to commercialise stem cells there are procedures and ideas which would never have been allowed in other branches of medicine, which will just go ahead.

Finally, I think we also losing our international conscience and the diseases that are affecting mankind are really in Africa and so on; it's not necessarily the quest for immortality in the affluent western world. I think part of our social conscience has got to be that the science is addressing the right questions.'

Vision 3: A vision from a campaign group

Joanna Fowler

Director

Society for Human Dignity

Well I think science has always got to be looking to cure and it's always got to be moving forward, but moving forward in an ethically acceptable way. We're learning from the environmental concerns at the moment that we might have made quite a few mistakes in the past. So I think that there shouldn't be a presumption that science always advances – in an ethical sense.

So my main objection to this research is around the sanctity of the embryo - the sanctity of life. I'm opposed to any research using human embryos. I have absolute respect for human life from the moment of conception, from the moment of the one cell embryo, and so any destructive research is something I would oppose, any deliberate intervention which destroys the human embryo, I would be opposed to.

I mean, you know, it always feeds back to the issue of necessity, doesn't it. How much of this work do you have to do? I don't know, this whole are seems to be driven relentlessly by scientists who don't want to accept any restrictions on the work that they're doing. I think the public are ill informed and, to some extent, manipulated by the media hype surrounding the potential cures within treatments that may be discovered using those embryonic stem cells.

I think the focus should be on adult stem cells or stem cells from cord blood. Now you never know for sure what the long term outcome will be - but it still looks to me like this is really where we should be putting some solid investment, and I get very, very frustrated that so little of what's going on in cord blood stem cells gets the media headlines. It amazes me how much hype they dangle in front of the public when it suits embryonic stem cell research. You know - embryonic stem cell claims are hypothetical at the current stage of research; adult stem cells are not only working but can differentiate.

So it's not just the ethics of the dignity of the embryo, I think it's even the ethics of research and investment. People seem to think that generally there's all this money, unending supplies of money that can go in every direction, but there isn't, and so there has to be choices. The public money side of it is extremely important, because then you get back to the fact that the tax payer contributes to this, and perhaps they should be involved and interested and even, you know, have rights to raise the ethical issues.'

Vision 4: A vision from a scientist

Dr Mary Hanrahan

Director Stem Cell Laboratories

University of Stratford

'How you deliver these therapies, you know, to everyone in a cost effective manner, not just for rich people who kind of avail themselves of these therapies, but how they really are available to everyone. I think that's our big challenge.

I got into this area because I think stem cell therapy is hugely important. I think it is a way of beginning to treat the underlying causes of the disease, not just the symptoms.

But to take that really forward, particularly on a grand scale within the NHS, I think it is going to take considerable Government resources and, you know, really quite pragmatic thinking. I mean, the infra-structure that will be required to try and deliver these kinds of therapies to very, very large numbers of people will require some very expensive outlays by the Government just to set up facilities to do that. So my vision would be that this science is for everyone – not for the few.

To get there we need both avenues of research – adult stem cells and embryonic. Adult stem cells are already used in a number of treatments. If you are using the patient's own stem cells you avoid a lot of the issues that come from using embryonic stem cells which are all to do with transplantation rejection. And I think there is real potential for these cells reprogrammed.

But, at this moment in time, human embryo research it is certainly the only way forward for a number of serious conditions such as spinal cord injury, cardiac failure probably, but mainly things like neurological conditions which cannot be treated in any other way. And personally – to me – I don't think an egg cell is a human being. I mean, you need to think about the ethics of not treating these conditions.

That goes for the clinical risks too. Why should someone not be allowed the right to have a spinal cord therapy which has a 95% chance of curing them if it has a one in 10,000 chance of giving them a cancer? You need informed consent – but it should be up to the individual. So I guess that's the final bit of my vision. We have a society grown up enough to have a mature conversation about this'

Annex 5: Repeat IML Qs and feedback

Q20-26: Britain needs to develop its science to enhance its international competitiveness

Scientists seem to be trying new things without stopping to think about the risks

We depend to much on science and not enough on faith

I trust scientists to tell the truth

The media sensationalises science

Science is driven by business – at the end of the day it is all about money

- Agree strongly
- Agree
- Neither agree nor disagree
- Disagree
- Disagree strongly
- Don't know

Q27 How familiar are you with stem cell research?

- Very familiar
- Fairly familiar
- Not very familiar
- Not at all familiar

Q28: Which, if any, most closely describes your view about the use of human embryos for research?

- The use of human embryos for medical research is never acceptable
- I believe using human embryos for medical research is permissible to find treatments for serious diseases and fertility research, but not for other types of research
- The use of human embryos is always acceptable for all types of medical research
- I don't know

Q29 Overall, what has your experience of today been?

- Excellent
- Good
- Fair
- Poor

Q30 How do you rate the venue?

- Excellent
- Good
- Fair
- Poor

Q31 How do you rate the food and refreshments?

- Excellent
- Good
- Fair
- Poor

Q32-36

I enjoyed taking part in the workshop

The specialists treated all participants respectfully

I learnt something I did not know before

There was enough time to fully discuss the issues

The information handouts provided were easy to understand

- Agree strongly
- Agree
- Disagree
- Disagree strongly
- Don’t know

Stem cells workshop 2:

Time	Session and aims	Topic areas	Tools/Stimulus material
10.30 – 10.45 Whole group	*Session 1: Welcome and introduction* Introduce workshop Canvass unprompted views on stem cell sources	Welcome and overview of session Welcome from Research Council Representative Housekeeping and ground rules; mention evaluators Feedback from findings of workshop 1 Voting on attitudes regarding sources of stem cells	IML interactive voting See annex 1
10.50 – 11.30 Whole group	*Session 2: Presentation - Tissue-specific stem cells* Provide an understating of tissue-specific stem cells - namely those derived from adult, foetal and cord blood material	Presentation What are the sources of tissue-specific stem cells What are the uses and challenges of tissue-specific cells for research What are the ethics surrounding their production and how are they governed What applications have their been to date and what is their clinical potential Q&A Handouts adult stem cells cord blood foetal material Discussion with experts for clarification	Presentation by scientist/ ethicist or social scientist Handouts See annex 2
11.35-12.25 Small groups	*Session 3: Discussion – Tissue-specific stem cells* Explore views and wider ethics of tissue-specific stem cells	General discussion and points of clarification Views on tissue-specific cells and research Views on views on benefits and limitations of research Specific views on sources from: Adult stem cells	Scientist/ ethicist as resource for group

		Probe: Initial reactions Clinical uses to date Views on the limitations of adult cells – particularly isolation an growth Cord Blood Probe: Initial reactions Views on public versus private banking Views on impact of collecting blood on care/ NHS more broadly Foetal tissue Probe: Initial reactions Informed consent Its usefulness for research Market in foetal material for treatments Overall views on public value of tissue-specific stem cell research in general	
12.25	Lunch		
1.10-1.50pm Whole group	*Session 4: Presentation - Embryonic stem cells* Provide an understating of tissue-specific stem cells	Presentation: What are embryonic stem cells What are the uses and challenges of ES cells for research What the sources and some of the ethics surrounding their production What applications have their been to date and what is their clinical potential Q&A Handout on ES Stages of embryo development IVF Therapeutic cloning Hybrids Reprogrammed adult cells Discussion with experts for clarification	Presentation by scientist/ ethicist or social scientist Handouts See annex 3
2.00-3.05pm	*Session 5: Discussion –*	IVF Probe:	Diagrammatic hand outs of ES

Small groups	*Embryonic stem cells* To understand public views in relation to sources of ES cells and discuss current regulatory issue	Initial reactions Views on differences on donated and created embryos Necessity Should IVF embryos be donated for research Should IVF embryos be created for research Should we use stem cell lines developed from embryos for things like: drug toxicity testing to help reduce the use of animals in research; Dentistry – by creating the means to grow teeth Therapeutic cloning Probe: Initial reactions Hype and availability of treatments Views on wider implications – e.g. reproductive cloning Necessity Should embryos be cloned for research Animal-human Hybrids Probe: Initial reactions Is it morally right to make an embryo with human and animal DNA Does the shortage of human eggs make means that this area should be prioritised Does a true mix of DNA between animals and humans cause any additional concerns Should human-animal hybrids be created for research? Re-programmed adult cells Initial views Does it make embryonic research necessary Discussion of extent to which (if at all) embryo research should be permitted for medical purposes Reflecting on day - should research into adult and cord blood stem cells be pursued instead of embryo stem	cells sources and legal context Scientist/ ethicist as resource for group

		cell research, or as a parallel route?	
3.05-3.15	Break		
3.15-3.30 Whole group	Session 5: Feedback, voting and thanks To review key thoughts from the day To track impact of discussion on views To explain what happens next	Feedback 3 top issues for the day from each group Voting on questions of support for research using TS cell and ES cells Completion of evaluation sheets	IML voting on key tracking questions See annex 4
3.30pm	Ends		

Annex 1: IML voting

Q1: Which, if any, most closely describes your view about the use of human embryos for research?

- The use of human embryos for medical research is never acceptable
- I believe using human embryos for medical research is permissible to find treatments for serious diseases and fertility research, but not for other types of research
- The use of human embryos is always acceptable for all types of medical research
- I don't know

To what extent do you agree or disagree with scientists using the following sources of stem cells for research

Q2: Using surplus embryos from IVF treatments

Q3: Using stem cells derived from umbilical cord blood

Q4: Using stem cells derived from aborted foetus

- Agree strongly
- Agree
- Neither agree nor disagree
- Disagree
- Disagree strongly
- Don't know

To what extent do you agree or disagree with scientists creating embryos from the following sources for stem cells research

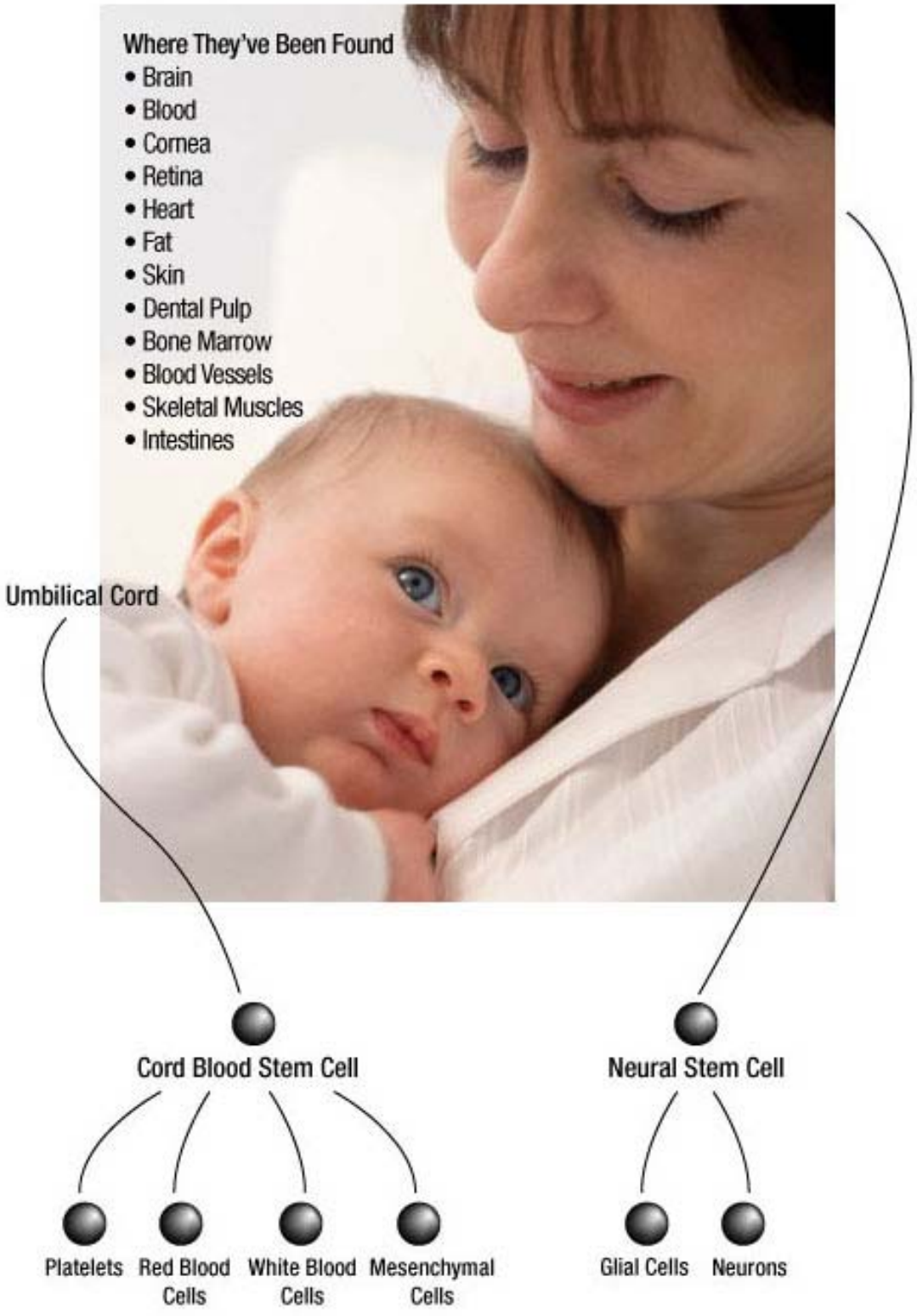
Q5: creating embryos by IVF methods specifically for research (i.e. people donating sperm and eggs for this purpose)

Q6: creating a human embryo by *cloning* methods

Q7: creating an embryo which contains mostly human with a small amount of animal genetic material by cloning methods

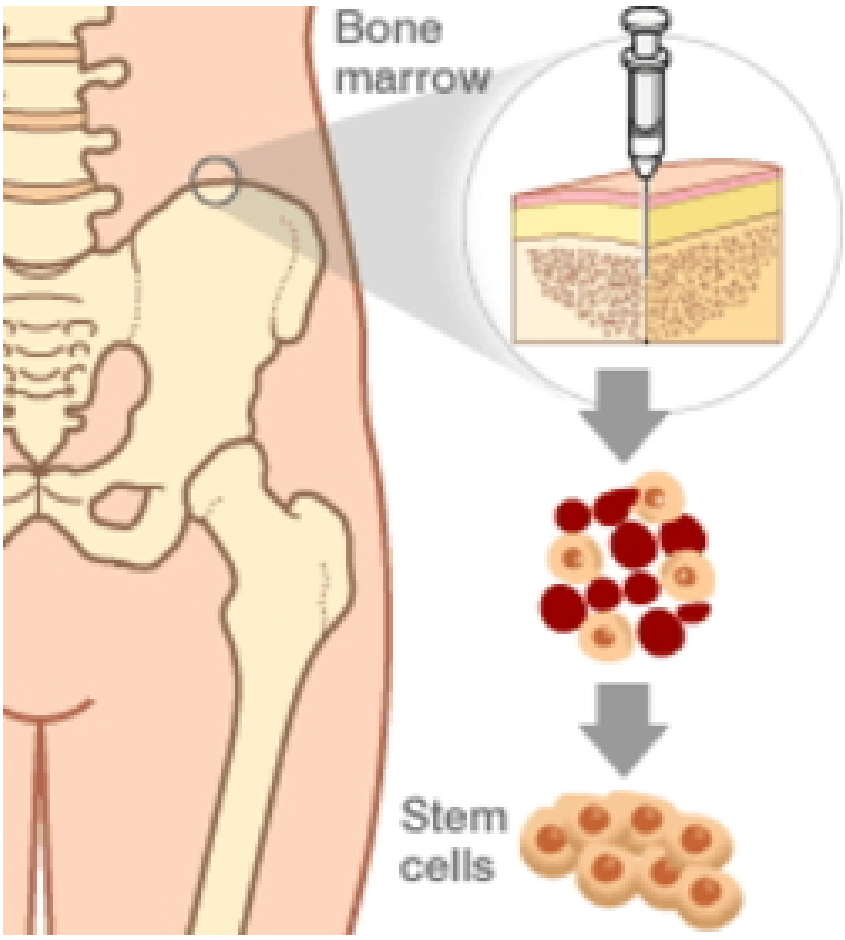
- Agree strongly
- Agree
- Neither agree nor disagree
- Disagree
- Disagree strongly
- Don't know

Annex 2: Where are Adult and Cord Blood Stem Cells Found?



Adult stem cells

Adult stem cells are found in all of our bodies in areas such as the eye, the bone marrow, muscle and the brain. Their job is to replace and replenish cells that are continually lost by depletion and damage. They are used therapeutically for a number of treatments including bone marrow transplants and skin grafts. However, unlike embryonic cells, they can naturally only give rise to a limited number of cells. They are also difficult to isolate and grow in the laboratory – making it hard to develop cheap and accessible therapies for everyone.



Stem Cells from Bone Marrow

Cord blood

Cord blood derived stem cells are collected from the umbilical cord and placenta at the birth of a baby. Cord blood is a particularly rich source of haematopoietic (blood) stem cells. Such haematopoietic stem cells have been used to treat a number of blood and immune-system related genetic diseases, cancers, and disorders – particularly in children. Researchers are now looking at the use of cord blood stem cells for regenerative medicine – for instance they have been used to make liver tissue. Cord blood cells are viewed as more plastic than adult cells. However further research is needed to establish their true potential.

There are already a number of services that bank cord blood. In the UK cord blood banking of has been undertaken largely by the NHS. Women in selected maternity units in the UK are approached during the antenatal period and offered the option to donate cord blood to the NHS Cord Blood Bank (NCBB). Appropriate consent is obtained. These donations are sent to the NCBB for processing and storage for future potential use in unrelated transplantation, in a similar way to bone marrow donations (there are issues of tissue rejection from this source).

Commercial services also offer mothers the opportunity to store their own baby's cord stem cells long-term, in case that child or his/her siblings ever develop diseases that could only be treated by cord blood stem cell transplantation – though the risk of this is very low. In addition, commercial cord blood banks are now marketing the potential use some cord cells – present in extremely low frequency - may have the capacity to develop into things like cartilage, fat cells, and heart cells. Research is still at an early stage and despite the amount of interest in the field the therapeutic role for such cells remains speculative.

In addition to these issues, there are concerns that such procedures may get in the way of either the midwife or other medical staff being able to give full care to the mother and child. New regulations have been brought in to ensure appropriate training by staff for the safe collection of cord blood.

Foetal tissue

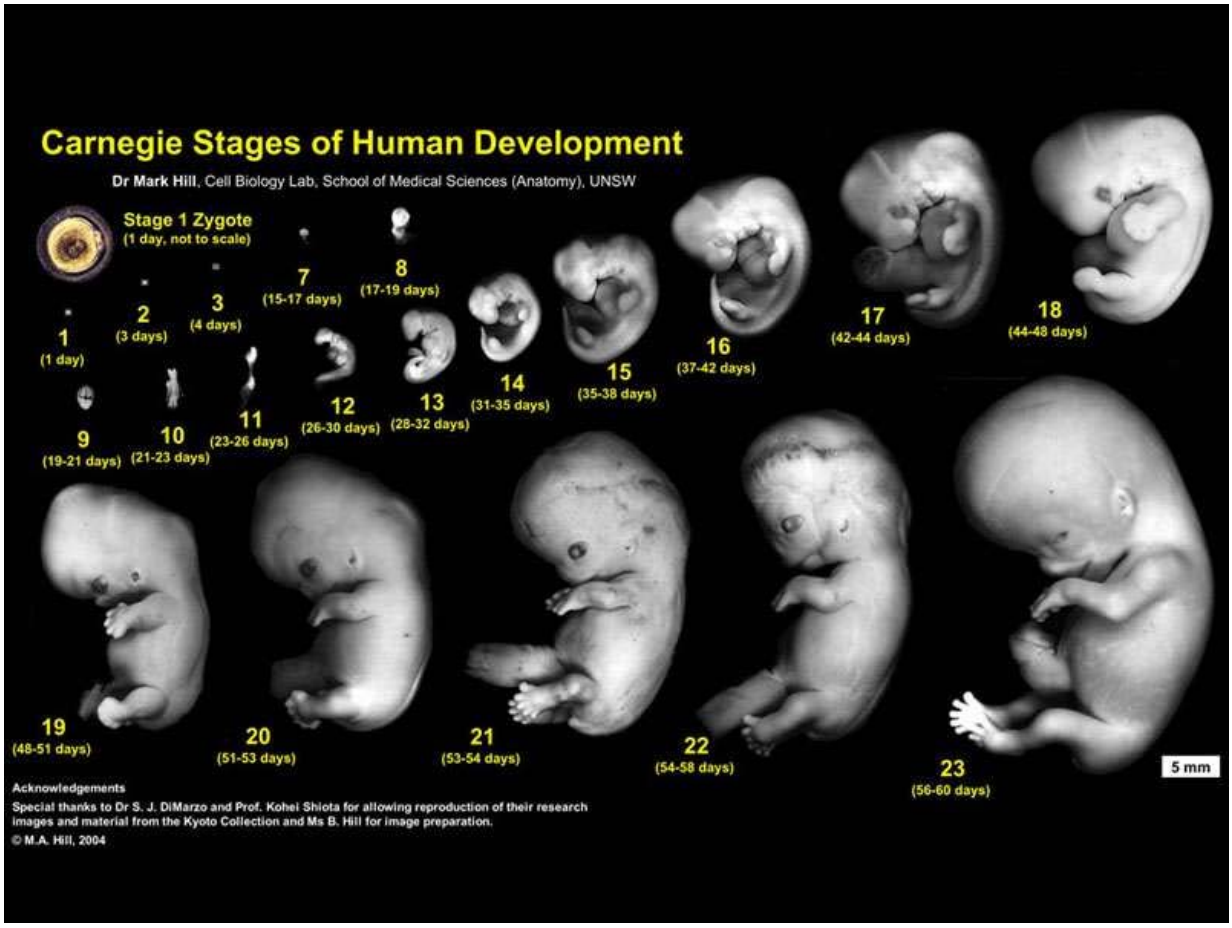
Stem cells can also be derived from the tissues of foetuses that have been aborted or miscarried. Foetal stem cells are being used to explore treatments for neurodegenerative conditions eye conditions and spinal cord injury – though these tissues will not match the patient and again risk rejection.

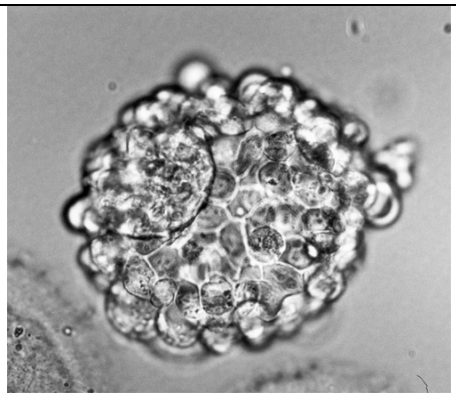
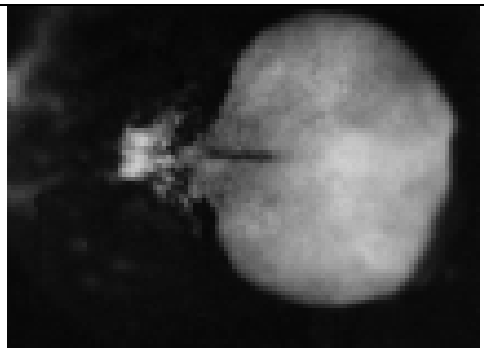
In the UK, the collection and use of aborted foetuses for research purposes is governed by the Polkinghorne guidelines. The guidelines are meant to prevent the deliberate conception and termination for treatment of a particular person – for instance by separating decisions relating to abortion and the subsequent use of the tissue, and by not allowing the donor to specify how her foetal tissue may or may not be used.

Rev. Dr. John C. Polkinghorne, KBE, FRS

However, there is concern around the amount of information being given to women when consenting to the use of aborted foetuses in stem cell research – in particular knowledge about the specific research uses the material and the right to agree to the foetus being used in some projects but not others.

Human Embryonic Development



	
Blastocyst 5-7 days	Embryo at 15-17 days Primitive streak developing – this is the site of formation of the 3 tissue layers - ectoderm, endoderm, and mesoderm

Embryonic stem cells

Embryonic stem cells have the potential to give rise to all the cells in the human body. They can also make copies of themselves – or self renew. However, date there no therapeutic treatments from embryonic stem cell research – indeed the first embryonic stem cells for research were not created in the UK until 2001. However, clinical trials for certain treatments are close (for instance applications are currently being considering in the US). Research is also widely used to create tissues to study disease.

The key challenge for developing treatments from embryonic cells is to control their differentiation – for example, scientists must learn how to direct stem cells to make muscle cells for damaged hearts or neurones to treat brain diseases and so on. Scientists also have to learn how to make sure that stem cells do not multiply in an uncontrollable way and create tumours.

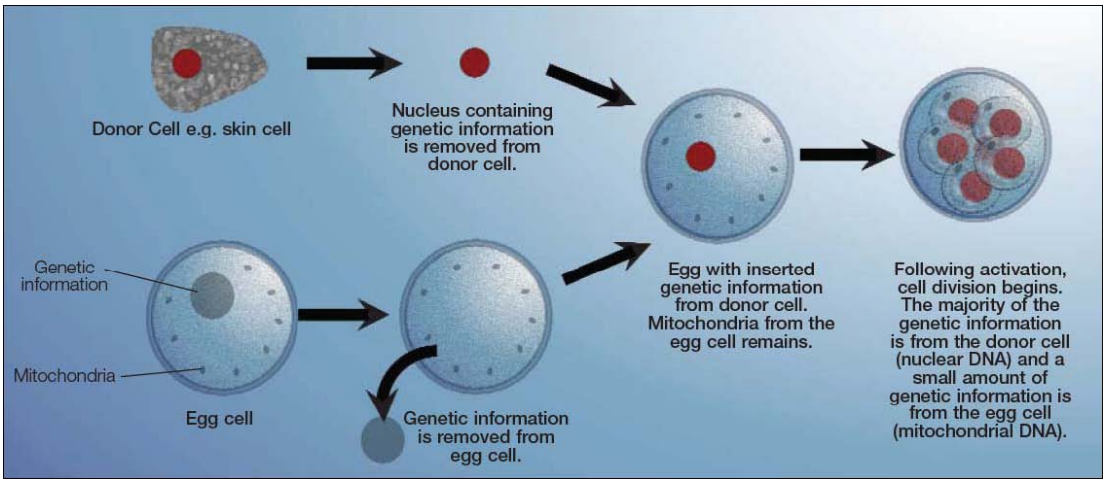
The most common source of these cells is from embryos left over from IVF treatments. Most IVF cycles produce more embryos than can be implanted back into a woman, leaving unwanted embryos which are normally frozen for later use, donated or discarded. Also embryos can be created that are not deemed to be of sufficient quality to be implanted. Such embryos are only used for research if the couple has given their consent. There is debate as to whether people should be able to use IVF procedures specifically to create embryos for research purposes. Stem cell lines generated from IVF will not match the tissues of the patient – and so present issues for tissue rejection.

Embryos stored in liquid Nitrogen

Embryo research is contentious as the development of stem cell lines from these sources predominantly involves the destruction of the early stage embryo, called the blastocyst. Critics have also argued whether embryonic research is necessary given that the therapeutic advances made in stem cell research to date have been from adult and cord blood stem cells. However, it should be noted that work on adult stem cells has been going on for decades, while scientists have only been working on embryonic stem cells for a much shorter time.

Therapeutic cloning

Therapeutic cloning has the potential to create copies of a patient's healthy cells to replace or repair damaged or diseased tissues and organs. It involves removing the nucleus from a donated egg and inserting the patients DNA into this 'empty' egg. The egg-cell combination is then stimulated (given an electric shock) to develop into a blastocyst, from which embryonic stem cells can be extracted after five days of growth. Because the stem cells produced match the patient's cells, therapeutic cloning offers the potential of growing tissue that is not rejected by the patient – though there is scepticism as to whether patient specific therapies could be affordable on a large scale.



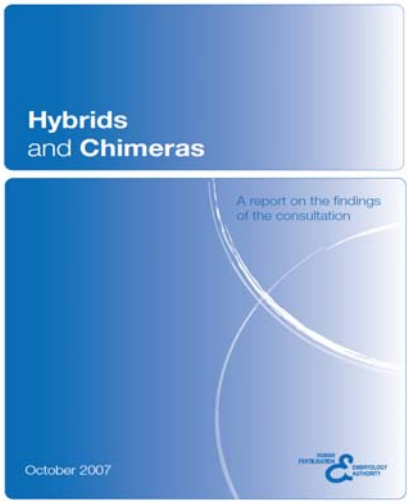
Currently, therapeutic cloning is extremely inefficient, with a success rate in animals currently less than 0.1%. Human embryos have recently been cloned in the US – though stem cell lines have not derived from this technique yet.

Therapeutic cloning is legal under UK Law. Scientists can apply for a license to clone human embryos provided they intend to use them to study disease in a laboratory situation only. The cloning of human embryos with the intention of creating a baby - reproductive cloning - is still strictly banned in the UK. As well as concerns about embryonic research in general, certain groups are also uneasy about therapeutic cloning as it could help perfect techniques that can be used for human reproductive cloning.

Human and animal hybrids

Following the same principles as for therapeutic cloning, it is possible to remove the nucleus from an animal egg and replace with human DNA to make human-animal hybrid embryos. Scientists aim to generate stem cell lines from these embryos, to help understand certain diseases such as Alzheimer's disease, Parkinson's and Motor Neurone Disease.

The Human Fertilisation and Embryology Authority (HFEA) have recently given the go ahead for this type of research and Britain's first human-animal cytoplasmic hybrid embryos have been recently created by a team in Newcastle - by inserting human DNA from a skin cell into a hollowed-out cow egg. This creates an embryo which has mostly human DNA with a small amount of animal DNA.



The HFEA Report Published 5th September 2007

Researchers want to use this technique due to the lack of human eggs for this type of research. The embryos are used as tools for research purposes only and are not implanted.

This technique has caused a great deal of controversy recently, with the Catholic Church in particular objecting to the notion of putting human and animal DNA in the same entity. Other commentators have argued that such research is not necessary – given the progress made in deriving stem cell tools from other sources.

Finally, the law currently does not permit creating embryos with a true mix of DNA between humans and animals. However, the Draft Human Fertilisation and Embryology Bill (currently going through Parliament) permits human-animal hybrids to be created for research but only under a licence from the HFEA. There are currently no applications to do this for research purposes.

Reprogramming adult cells to have embryonic like properties

To overcome this, recent research has focused on how to reprogram adult cells to mimic embryonic stem cells. Scientists have successfully reprogrammed adult skin cells to an embryonic like state by adding four genes; the scientists then stimulated the cells created to produce brain and heart tissue. While these cells are like embryonic stem cells in that they have the potential to form all different types of cells in the body - they are not an embryo. The cells would not be able to develop into a foetus.

November 2007— Acclaimed stem cell researcher Shinya Yamanaka, MD, PhD, reports that he and his Kyoto University colleagues have successfully reprogrammed human adult cells to function like embryonic stem cells.

At present this work is best thought of as a research tool rather than a therapy - since numerous safety issues will need to be addressed before they can be used clinically. For instance, at present techniques rely on viruses to introduce new material into the cells, which carries a potential risk of contamination. However, such techniques could potentially lead to stem cell treatments that can match the tissues of the donor, minimising the risk of rejection.

Annex 4: Repeat IML voting

Q8: Which, if any, most closely describes your view about the use of human embryos for research?

- The use of human embryos for medical research is never acceptable
- I believe using human embryos for medical research is permissible to find treatments for serious diseases and fertility research, but not for other types of research
- The use of human embryos is always acceptable for all types of medical research
- I don't know

To what extent do you agree or disagree with scientists using the following sources of stem cells for research

Q9: Using surplus embryos from IVF treatments

Q10: Using stem cells derived from umbilical cord blood

Q11: Using stem cells derived from aborted foetus

- Agree strongly
- Agree
- Neither agree nor disagree
- Disagree
- Disagree strongly
- Don't know

To what extent do you agree or disagree with scientists creating embryos from the following sources for stem cells research

Q12: creating embryos by IVF methods

Q12: creating a human embryo by *cloning* methods

Q14: creating an embryo which contains mostly human with a small amount of animal genetic material by cloning methods

- Agree strongly
- Agree
- Neither agree nor disagree
- Disagree
- Disagree strongly
- Don't know

Q15: Reflecting on day - should research into adult stem cells be pursued instead of embryo stem cell research, or as a parallel route, or not at all?

- instead of embryo stem cell research
- a parallel route
- not at all
- Don't know

Workshop 3: Stem cell applications

Topic Guide

Time	Session and aims	Topic areas	Tools / Stimulus material
10.30-11.00 Whole group	*Session 1: Welcome and introduction* *Whole group* Introduce session Canvass unprompted individual views Highlight different perspectives on stem cell banks	Overview of workshop Overview of basic definitions and findings from workshops 2 IML voting Presentation on stem cell banking Q&A	IML interactive voting Scientist and Social scientist presenting
11.05-11.35 Break outs Small groups	*Session 2: Stem cell banks* *Small groups*	Initial views on development of stem cell lines for research and therapies Views on number and type of lines banked to date	Handout 1: UK stem cell bank Scientist/ ethicist as resource for

	Understand views on the governance of stem cell banks and development of stem cell lines	What research ethics and safety issues should govern the banking of stem cells? Views on ethics of donation (ivf/ created/ foetal/ adult)? Should we allow the patenting of human stem cells lines and does free access impact on commercialisation? Equality and access to stem cell lines and treatments? Who should pay for the costs of stem cell research and treatments?	group
11.40-12.10	*Session 3: Presentation on applications of stem cells* Whole group To highlight current research and potential clinical applications	To cover basic research Drug discovery Oncology Current clinical uses Potential uses and risks Q&A	Scientist and Social scientist presenting
12.15-	*Session 4:*	What do you feel about some of the	Handout 2:

12.50	*Research and potential therapeutic uses* *Small groups* To understand how the public value potential uses of stem cell research and clinical practice	potential areas of research? Views on uncertainties in science What views do you have about the value of: Basic research • Probe current uncertainties Drug testing • Quick wins • Ethics of uses of embryonic stem cell lines for drugs Clinical treatments • Uncertainties in science • Length of time to clinic Understanding of cancers for effective drug therapies • Probe views on use of stem cells as a diagnostic tool Trade offs and costs required • Investment in infrastructure to support therapies • Tax Do you feel that hype around the therapies may lead to patient disappointment	Research and therapeutic uses Scientist/ ethicist as resource for group

		Preference overall for using stem cells to understand diseases to inform treatments – versus therapeutic use	
12.50	*Lunch*		
1.30-2.25	Session 5: Patients, safety and clinical trials *Small groups* To explore some of the benefits and risks of stem cells treatments from a patient perspective	<u>Handout 3:</u> Views overall Views on risks of terratoma/ cancer Views on which patients should be prioritised • Terminal diseases older people • Diseases of younger people • Other suitable therapies Views on right to compensation if experimental trials go wrong • Relate to patient groups as above Views on medical tourism Views on scientists practicing with experimental treatments outside of UK regulations	Handout 3 and handout 4

		Would a 'scare story' impact on peoples trust in the science Should experimental treatments be offered to terminally ill patients <u>Handout 4:</u> General views What is peoples understanding of a clinical trial Should placebos be used or the best other available treatment Views on risks of therapies Is there a risk of hype surrounding stem cells leading people to undertake risky trials	
2.25 – 2.40	*Break*		
2.40 – 3.00	*Session 5: Reflections on day and workshops*	What has surprised you most about today?	

	overall To understand which issues influenced views To understand information needs To understand key messages for decision makers, scientists and other groups	Have people change their minds a result of discussion? What key thing has influenced your view? What has not changed and why? What information do they feel people need to make judgments on ethics of stem cell applications Thinking back across the study what are the key messages for: Policy makers For scientists For wider stakeholder groups, such as campaign and church groups	
3.05	*Session 6: Reflections on the workshop and dialogue overall* To track impact of discussion on views relating to applications	Feedback Top three issues from groups IML voting Explain reporting process, opportunities for feedback and policy workshop later in year	IML Voting

	To gain feedback on key messages for policy makers and scientists Next steps	Thank and close	
3.30	*Ends*		

Annex 1: IML voting

Which, if any, of the following would you say were a high medium or low priority for future in investment in stem cell research and clinical practice?

Q1. Stem cell banks to develop tissue lines that may be used for research and clinical practice?

Q2: Basic research into cell behaviour

Q3: Research into the early diagnosis of diseases

Q4: Research into therapies for diseases

Q5: The use of tissue lines from stem cells for drug development

Q6: Research into the biology of diseases such as cancers, to increase the effectiveness of drugs and treatments

- High
- Medium
- Low

Q7: And if you had to prioritise three areas, which would they be (press three choices only):

1. Stem cell banks to develop tissue lines that may be used for research and clinical practice?

2: Basic research into cell behaviour

3: Research into the early diagnosis of diseases

4: Research into therapies for diseases

5: The use of tissue lines from stem cells for drug development

6: Research into the biology of diseases such as cancers, to increase the effectiveness of drugs and treatments

Annex 2

Handout 1: The UK Stem Cell Bank

The UK Stem Cell Bank opened in 2004. The first of its kind in the world, the bank is responsible for storing, characterising and supplying ethically-approved, quality-controlled stem cell lines for medical research and treatment from the UK and overseas.

The Bank is a repository for human stem cells derived from adult, foetal and embryonic tissues. The UK's first two human embryonic stem cell lines were approved for deposit in the bank in May 2004. Four years later, 65 lines had been approved for banking. Of these, 54 are in the bank, 10 are of research grade quality and none are clinical grade quality. The first clinical grade lines are expected in two years.

An independent Steering Committ evaluates all applications to deposit and access cell lines. Requests for deposits access must show that all ethical approva licences and authorisations are in place.

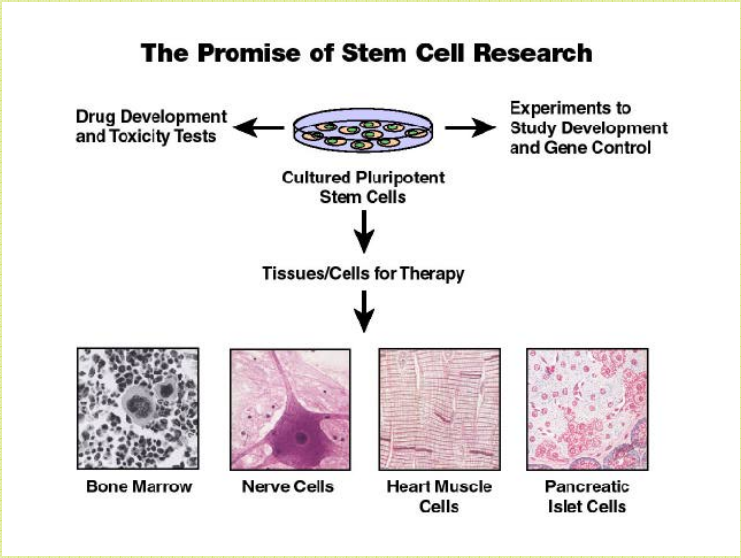
There are a number of rules concerning information to be given to potential donors and consent requirements. Donors are asked to gift their stem cells, relinquishing all future control, after information is provided about the implications of doing so.

It has been suggested that the UK Stem Cell Bank should seek to build up a collection of clinical-grade stem cell lines representing a range of different tissue types, with the aim of being able to provide immunologically-matched lines for as many patients as possible.

It has been estimated that cells from 150 random embryos would, on average, be enough to provide the best possible match for 13% of recipients, a favourable level of match for 65%, and some use for as many as 85%. It is possible, however, that despite good intentions such repositories may fail to include the less common tissue types, thus potentially disadvantageing minority racial and ethnic groups. To address this, either more stem cell types would need to be generated from these groups or the Bank would need to collaborate with other stem cell banks around the world – which may forge wider issues for safety and governance.

Handout 2: Research and potential therapeutic uses

Whilst there are a number of potential research and therapeutic uses of stem cells, at this stage it is difficult to know which diseases will benefit from stem cell research, which types of stem cells are ultimately likely to be of most value for each disease and how long cell therapies might take. Scientists are concerned not to over-state the potential benefits of therapies and raise expectations of patients.



I think there's a big issue about expectation with stem cells and there's one heck of a lot of basic research to be done. It's not just a question of, oh we've got a few stem cells, let's plug them into therapy

One of the key uses of stem cells is for **basic research** and to gain a better understanding of cell biology, such as how stem cells to self-renew and specialise into other cell types

Stem cells could also be a valuable aid in **drug testing**. Large numbers of a particular type of cell could be grown and used to screening potential drugs for toxicity or their impact on a disease. This could reduce the need for animal testing.

Some of the big advances with stem cells will not be in the clinical application side, but on less sexy things like drugs

Handout 2 Continued:

It will be very complicated to replace brain tissue, and to get stem cells to wire and make the right connections.

In terms of **therapies**, bone marrow transplantation and umbilical cord blood stem cells have been used successfully for the treatment of leukaemia, non-Hodgkin's lymphoma and various inherited blood disorders. Immature nerve cells from aborted human fetuses have been transplanted into the brains of people suffering from Parkinson's Disease and Huntington's Disease, but with mixed success.

Early-phase clinical trials are being planned around the world to test whether adult stem cells (mainly bone marrow cells) can be used to treat heart attack, musculoskeletal problems, liver disease, immune disorders, cancers, diabetes, multiple sclerosis and spinal cord damage. The first clinical trial involving human embryonic stem cells is likely to start this year in the US.

Stem cells are also used as a research tool (rather than a therapy) to understand disease. Because of similarities between cells that form tumours and stem cells, they are very useful in **understanding cancers.** This may help in early diagnosis and treatments.

If they are looking at the stem cells as a model for cancer and try to understand the mechanisms so that they can inhibit them, then I think that is entirely reasonable. But if they are thinking of injecting stem cells into a patient to somehow overcome the cancer, I just can't see how it could possibly be helpful.

Handout 3: Safety and patients

Many serious diseases have been suggested as possible candidates for stem cell therapy. New therapies can carry considerable risks, and the potential complications and dangers of stem cell therapy are serious, including tumour formation, infection and immunological complications – these are hard to test in vitro (outside of the body). A parallel example is gene therapy work that was undertaken for children with genetic diseases of their immune systems. They were treated with a viral therapy to replace the gene that they were missing, but it caused tumours and a number of children got leukaemia.

It could be argued that the priority for stem cell transplantation studies should be terminal diseases of older people, such as late-stage Parkinson's disease or Alzheimer's disease.

On the other hand, a greater number of life-years would be gained from successful treatment of younger people suffering from autoimmune diseases such as Type 1 diabetes or multiple sclerosis, or from brain injury. Where no other treatment is available, high-risk experimental treatments are easily justified but if, as in the case of Type 1 diabetes, relatively effective therapies are available, the decision to enrol children or young adults in clinical trials of stem cell therapies is a serious one. There are also issues concerning liability and compensation if a patient is harmed by a these therapies.

Many people suffering from terminal or debilitating diseases, fearing that the time available to them for treatment is limited, have been travelling to other countries, such as Russia, India or China, to take advantage of untested stem cell therapies. There are no regulatory bodies to monitor these treatments; no data is published in peer reviewed journals to enable others to replicate any results.

Handout 4: Clinical trials

For clinical studies on stem cell therapies, it will be important to dampen any unrealistic expectations in prospective participants. For instance, patients offered the opportunity to participate in clinical trials sometimes believe, despite explanations to the contrary, that research is designed to benefit them directly rather than to test or compare treatment methods. Despite understanding the concept of placebos, they often persist in a belief that they will receive the treatment most likely to benefit them during a trial.

Careful consideration will also need to be given to the design of clinical studies. Although blind randomized controlled trials - where you test the drug randomly to a placebo without the patient knowing the treatment group - is the gold standard for clinical trial, from an ethical perspective it may be problematic for early-stage stem cell studies.

For example, criticism has been levelled at foetal neural cell transplant trials that were conducted in patients with Parkinson's disease in the US. Patients in the placebo group were subjected to neurosurgery that involved drilling holes into their skulls – despite there being no clinical benefit treatment associated with the surgery.

It has been argued that where the experimental treatment involves invasive surgery – as it will in many applications of stem cell medicine – the control treatment should not be placebo surgery but the current clinically approved treatment and standard of care. This may however forge other issues, particularly when existing treatments may carry risks and may not be very effective.

Annex 4: Repeat IML voting

Which, if any, of the following would you say were a high medium or low priority for future in investment in stem cell research and clinical practice?

Q8. Stem cell banks to develop tissue lines that may be used for research and clinical practice?

Q9: Basic research into cell behaviour

Q10: Research into the early diagnosis of diseases

Q11: Research into therapies for diseases

Q12: The use of tissue lines from stem cells for drug development

Q13: Research into the biology of diseases such as cancers, to increase the effectiveness of drugs and treatments

- High
- Medium
- Low

Q14: And if you had to prioritise three areas, which would they be (press three choices only):

1. Stem cell banks to develop tissue lines that may be used for research and clinical practice?

2: Basic research into cell behaviour

3: Research into the early diagnosis of diseases

4: Research into therapies for diseases

5: The use of tissue lines from stem cells for drug development

6: Research into the biology of diseases such as cancers, to increase the effectiveness of drugs and treatments

How much do you disagree or agree with the following statements that people have said about science.

Q15-20: Britain needs to develop its science to enhance its international competitiveness

Scientists seem to be trying new things without stopping to think about the risks

We depend to much on science and not enough on faith

I trust scientists to tell the truth

The media sensationalises science

Science is driven by business – at the end of the day it is all about money

- Agree strongly
- Agree
- Neither agree nor disagree
- Disagree
- Disagree strongly
- Don't know

8 Appendix 4: Q methodology results

Analysis of the small number of 'expert' Q sorts that were returned revealed two distinct perspectives: the first, which we have labelled the 'Scientist' perspective, was defined by the Q sorts of the four scientific researchers who responded; the second, which we have labelled the 'Ethicist' perspective, was defined by the Q sorts of the two individuals concerned with ethical and social aspects of stem cell science. As Table 1 shows, two of the four scientists also had a significant negative loading on the Ethicist factor, indicating a degree of polarisation of views between the Scientists and the Ethicists on some of the statements included in the Q sorts. A slightly larger sample of expert data would very likely reveal further nuances in these broad viewpoints but for the purposes of this study this small sample served well enough. As already noted, the main purpose of analysing the expert Q sorts was to utilise the output for purposes of comparison with the results of the analysis of Q sorts completed by the lay workshop participants; these two distinct factors provided a broad representation of 'scientific' and 'ethical-critical' expert viewpoints for incorporation in the second-order analysis of the participant data.

Table 6: Expert Q-sort factor matrix showing significant loadings

Q sort	Expert research focus	Factor Loadings	
		1	2
Expert 1	Clinical	**0.84**	
Expert 4	Basic	**0.81**	
Expert 2	Basic &Therapeutic	**0.74**	-0.52
Expert 3	Basic & Therapeutic	**0.70**	-0.50
Expert 5	Ethical & Social		**0.94**
Expert 6	Ethical		**0.88**

The analysis of the Q sorts completed by the workshop participants identified three factors representing distinct shared points of view. The retention of three factors was indicated by the criterion, widely used in Q methodology research, that there should be two or more significant loadings on each factor, as well as according with the more generally used factor analytic heuristic that factors with an Eigenvalue less than 1 be discarded. A four factor solution was also examined but the fourth factor represented a point of view defined by only a single

individual and was therefore, for the purposes of this study, excluded from the analysis. Table 3 displays the factor matrix, for clarity showing only significant loadings on each factor. It can be seen from the matrix that Factor A, which we have labelled 'Confident Support', is defined by the Factor 1 sorts extracted from the analysis of each of the five sub-samples of participants, which was in each case also the factor that had most individuals associated with it. It can be seen from the matrix that the 'expert' Factor 1 (the 'scientist' viewpoint) also loads strongly on Factor A. This indicates that the views of the workshop participants loading on Factor A correspond in may respects to those of the research scientists. Although Q methodology does not lend itself to making statistical generalisations about the distribution in the wider population of the views identified, the mode of analysis employed in this study demonstrates that a broadly similar view appears consistently among participants across all workshop locations.

Table 7: Rotated factor matrix showing significant factor loadings

Q Sort	Factor Loadings		
	Factor A	Factor B	Factor C
Edinburgh Factor 1	**0.91**		
Newcastle Factor 1	**0.91**		
London Factor 1	**0.89**		
Bristol Factor 1	**0.87**		
Cardiff Factor 1	**0.87**		
Expert F1 ('Scientists')	**0.79**		
Cardiff Factor 2		**0.82**	
Expert F2 ('Ethicists')		**0.76**	
Edinburgh Factor 2		**0.71**	
Newcastle Factor 2			**0.84**
London Factor 2			**0.81**

As can also be seen from Table 2, Factor B, which we have labelled 'Ethical Criticism', is defined by the Factor 2 sorts that emerged from the sub-samples from two of the locations, Cardiff and Edinburgh, as well as by Factor 2 from the expert Q sorts, the Ethicist perspective. Finally, Factor C, which has been labelled 'Selective Acceptance', is defined the Factor 2 sorts produced by the sub-samples from London and Newcastle. The following paragraphs provide a characterisation of the three perspectives represented by these factors, based on the normalised factor scores. The ranking given to each statement by factor is shown in Table 3 at the end of this summary.

Factor A: Confident Support

The point of view captured by Factor A expresses a confident view of stem cell science, emphasising the enormous benefits that the research promises and supporting the use of stem cells for basic as well as for therapeutic research, and rejecting various ethical objections.[5] A summary of the highest and lowest scoring statements for this Factor is given in Table 4 below. It maintains that continued research with human embryonic stem cells (hESC) is necessary in light of the therapeutic limitations of adult stem cells, correspondingly rejecting the proposition that adult SC research is already delivering effective treatments and that hESC research is of limited value. The ethical argument that embryos should not be used for research purposes at any stage of development is also rejected because an embryo of less than 14 days development is not seen as having personhood. Similarly, this viewpoint does not accept the argument that the creation of embryos for research purposes involves the destruction of a life, as the embryos would never be implanted in a uterus. The idea that the creation of hybrid animal-human cells is unnatural and therefore risky is also dismissed. The use of donated 'spare' embryos from IVF is endorsed, as is the use of foetal tissue, although it is emphasised that the storage of gametes or embryos should be subject to the active, informed consent of the donor. It is nevertheless acknowledged that the possibility of creating stem cells from adult tissues may avoid some of the ethical issues surrounding the use of embryonic cells.

There is no support for the argument that business should be able to patent inventions based on human embryonic stem cells. On the other hand, there is acceptance that the establishment of commercial stem cell banks for storing cells extracted from the umbilical cord is ethical and not exploitative of parents' concerns; even if there were only a very small chance that stored tissue would later provide a needed therapy for a child, it was seen as being worthwhile. Although not commenting on the question of payment for egg donation, this viewpoint accepts the idea that women who cannot afford IVF might be offered it for free in exchange for the donation of surplus eggs for research.

Equity issues are nevertheless a concern and it is stated that stem cell treatments should be available to all and not just to those who can afford to pay. However, the proposition that the money spent on developing costly therapies for the developed world would be better spent on meeting the far more basic needs of those in the developing word is rejected.

Underpinning the confidence expressed in this factor is a belief in the integrity of scientists and the effectiveness of the regulatory system to ensure that the research will not be misused. It is believed that the views of the public should be

[5] Numbers in parentheses

taken into account when regulating stem cell research but also that Government will listen.

Factor B: Pro life critics

This point of view is almost the polar opposite to that of Confident Support. A summary of the highest and lowest scoring statements for this Factor can be found in Table 5. The theme here is primarily the ethical rejection of embryonic stem cell research and a critical view of stem cell science as well as of scientists themselves.

The view that life should never be created to grow spare parts for another person and indeed that embryos, however they are sourced, should not be used for research purposes at any stage in their development is asserted very clearly. This perspective strongly rejects the claim that an embryo does not have personhood before the 14th day in its development or that because embryos created for research purposes would never be implanted their use does not constitute the destruction of a human life. It dismisses the argument that it is better to donate 'spare' embryos from IVF for use in research, rather than simply discard them, and similarly rejects the notion that the creation of hybrid cells is ethical and acceptable, even for research into treatments for serious diseases. In addition to a concern that all associated tissue donation should be the subject of active, informed consent, there are further ethical concerns about the relationship between stem cell research and IVF. These include the possibility that potential donors may feel themselves under pressure to donate at a very stressful time and a view that incentivising donation by offering payment or even by offering free treatment to women who cannot afford IVF if they donate their spare eggs is unacceptable. There is also strong opposition to the argument that businesses should be allowed to patent inventions developed from research that they have funded using human embryonic stem cells.

There are very significant concerns about the value and integrity of much stem cell science. There is emphasis on the claim that research with human embryos is premature and driven more by scientists' ambition and pursuit of professional glory than the most urgent medical need. There was also a view that certain scientists had a tendency to exaggerate what the science can deliver. With many of the benefits seen as being uncertain and far off, it is argued that it would be better to give priority to improving ways of treating and managing diseases that will benefit patients now. This is allied with the argument that the money might be better spent on meeting the basic health needs of large numbers of people in the developing world. There is also evident concern that scientists would be unable to prevent the potential misuse of their research and about the potential risks associated with embryonic stem cells, including hybrid cells. The suggestion that we can rely on scientists to develop stem cell science in ways that will be beneficial to society is therefore strongly dismissed.

Like the Confident Support Factor, there is strong support for the consideration of the public's views when regulating stem cell research but here it is allied with a lack of confidence in the expertise of regulators or the effectiveness of current laws.

Factor C: Selective Acceptance

The Selective Acceptance point of view is quite distinct from the other two, relatively polarised, viewpoints in that it expresses both support for stem cell science and ethical reservations about certain aspects of the research. Table 6 gives a summary of the highest and lowest scoring statements for this Factor. The main characteristic of this perspective is that it rejects the use of embryos, including hybrids, but strongly endorses adult stem cell research and the collection and storage of umbilical stem cells. The notion of a 14 day threshold in embryonic development is not accepted and there are concerns about the risks of creating hybrid cells. This point of view displays a high degree of confidence in the science, which it sees as holding out great promise and, and in the scientists, who are seen as being open, this latter view perhaps influenced by the experience of meeting several scientists in the course of the workshops. It also sees the uses of the science as being well controlled by scientists and subject to effective regulation, endorsing the involvement of non-experts in the regulatory process. There is also a belief that Government would be responsive to public views on this issue, although again this latter impression may have been shaped to some extent by the experience of involvement in the stem cell dialogue process.

This perspective also expresses the strongest opposition to the patenting by business of the products of research using human embryonic tissue. There is a strong view that stem cell research should be publicly funded in the public interest and not funded by private business. Nevertheless, the suggestion that commercial stem cell banks to store umbilical stem cells are unethical and simply playing on parents' fears is strongly rejected and the parental motivation to store such tissues, even in the face of a low probability of it resulting in an effective treatment for their child later in its development, is affirmed. In a position that may seem somewhat contradictory to the rejection of the use of human embryos, there is an endorsement of the right of women who donate eggs or embryos for research to some kind of recompense, whether payment or free IVF treatment.

Some point of general agreement

The preceding sections have outlined the views characterised by the three Factors but it may be useful to note a few points upon which there was an apparent degree of consensus.

Firstly, public input into regulatory decision-making was one issue on which there was clear accord between these different viewpoints, with all three asserting that

the views of the public must be taken into consideration when regulating stem cell research (2/3/2 respectively); this despite the fact that the Ethical Criticism perspective seems less certain whether Government will listen. There was, however, less overt support for the involvement of lay people in the regulatory process, with only the Selective Acceptance viewpoint rejecting strongly (-3) the argument that it is a mistake for them to be involved due to their lack of knowledge.

Secondly, there was broad consensus in the responses to the suggestion that businesses which invest in embryonic stem cell research should be able to patent the products of their investments. Unlike those statements that received relatively neutral scores (+1 / 0 /-1) across all three Factors, agreement here was not through indifference or uncertainty but through a clear rejection of the statement. Interestingly, the rejection of this proposition was strongest not in the Ethical Criticism Factor (-3) but in the Selective Acceptance Factor (-4), with even the Confident Support Factor scoring it at -2.

Thirdly, all three Factors rejected the view that there was too much conflicting information, which made it difficult to evaluate claims about stem cell science. This may in part reflect the fact that all participants had been exposed to three days of presentations and discussion on the topic. It may also reflect the fact that there has been relatively little controversy in Britain around stem cell science despite periodic media coverage of contentious issues, such as that generated by Parliamentary debates about the issue of hybrid cells. This contrasts with other bioscience such as agricultural biotechnology which have, in the past, been the focus of intense public debate and concern.

Finally, the set of statements included one about the use of stem cell research to develop skin treatments for cosmetic purposes. Despite the occasional coverage given to such stories in the popular press in particular, there was strong rejection across all three Factors that this should be encouraged, although there seemed to be little concern that the activities of overseas clinics apparently offering untried treatments of this kind might have a damageing effect on the reputation of therapeutic stem cell research.

Table 8: Statements used in the Q sort showing scores for each Factor

No.	Statement	Factor		
		A	B	C
1	Embryos created for stem cell research would never be implanted in a womb, so the argument that a potential human life is being destroyed is completely false as these embryos can never develop.	3	-4	-1
2	It is perfectly acceptable for women who can't receive infertility treatment on the NHS to be offered it for free in exchange for donating any spare eggs or embryos for research.	2	-2	2

3	The Government won't take any notice of public consultation about stem cell research. They already have their own ideas and agendas.	-2	1	-3
4	There is so much conflicting information about stem cell research it is difficult to know who or what to believe.	0	1	0
5	Stem cell research promises enormous benefits in terms of the development of new treatments for diseases that at present are difficult or impossible to treat.	4	0	2
6	The possibility of creating embryonic stem cells from adult tissue avoids the ethical issues that would result from use of stem cells from embryonic or foetal tissue.	2	1	4
7	Most of the people who claim that therapeutic cloning is wrong seem to have the wrong impression: we're talking about cloning cells, not people.	1	-1	1
8	The regulators just do not have the expertise to make properly informed decisions about some of the newer areas of stem cell research.	-1	1	-4
9	The use of human tissues grown from stem cells for the laboratory testing of drugs or other chemicals should be encouraged because it may lead to less animals being used in research.	1	-1	1
10	We cannot limit stem cell research because the future health of me and my children may well depend on scientists being able to work without fear of restriction.	0	-1	-1
11	It seems unsafe to put human DNA into animal cells to create hybrid cells that are impossible by natural processes. It seems risky to do something that nature prevents.	-2	2	3
12	Involving non-experts in the regulation of scientific research is a mistake. They do not have sufficient knowledge and understanding to make informed decisions.	0	-1	-3
13	I accept the need for stem cell research and the cells have to come from somewhere, but it is unacceptable to use cells taken from aborted foetuses.	-4	-2	4
14	Setting up commercial stem cell banks to store cells taken from umbilical cord blood is unethical. It just plays on parents' fears to make money.	-2	1	-3
15	Of course it's ethical to create so-called 'hybrid' cells. They would never become viable human beings. They just create stem cells to save having to use human cells.	1	-3	0
16	All embryos are human life and as such should not be used for research purposes at any stage in their development.	-4	4	1
17	If storing umbilical cord stem cells at birth gave even the smallest chance of a cure or life improvement for my children should they become ill in the future, I'd definitely go for it. What parent wouldn't?	3	-1	2
18	Many of the benefits promised by stem cell research seem very uncertain and far off. We should give priority to improving ways of treating and manageing diseases that will benefit patients now.	-1	3	0
19	No legislation will prevent therapeutic cloning research being exploited.	-2	0	-2
20	We have to continue research with embryonic stem cells because adult stem cell can only provide a limited range of therapies.	4	-2	-2
21	There is a tendency for some scientists to resort to hype and exaggeration about what stem cell research can deliver.	-1	3	0

22	We should encourage the use of stem cells to develop skincare treatments that keep you looking young.	-4	-3	-2
23	Eggs, sperm or embryos should only be stored with the active, informed consent of the donor.	3	2	0
24	An embryo less than 14 days old is not yet a person; it is just a bundle of cells and does not have the same right to life as a fully developed human being.	2	-4	-4

25	Stem cells should be used not just for therapies but for basic research to increase our knowledge about how the body works. This would benefit everyone.	2	0	1
26	Scientists seem quite secretive about stem cell research. I don't think that most people feel as though they are being informed.	-1	1	-2
27	Research with adult stem cells is already delivering effective treatments but I'm not convinced that embryonic stem cell research will prove that useful.	-3	-1	3
28	The science is developing so fast it seems as though it is getting out of control, and there is nothing we can do to stop it.	-3	0	0
29	Businesses invest large sums of money in stem cell research so they should be able to patent inventions based on human embryonic stem cells just like any other invention.	-2	-3	-4
30	The laws we have in place for governing embryo research are very effective in controlling the sort of studies that are carried out.	1	-2	-1
31	We can rely on scientists, the people with expert knowledge, to develop stem cell research in ways that will benefit us.	0	-4	1
32	Wealthy countries like Britain go to extreme lengths to prolong life for people while millions in the Third World die prematurely of conditions that don't require high tech solutions. The money would be better spent on them.	-3	2	-1
33	Stem cell research should be publicly funded for the public good – not by businesses for commercial profit.	1	0	3
34	Stem cell research is acceptable if it is intended to relieve suffering but not if it's just research for research's sake.	1	-1	1
35	The cosmetic treatments based on stem cells offered by some clinics in other countries are highly experimental and risk damageing the reputation of legitimate stem-cell research into curing illness.	1	0	-2
36	Infertility treatment is stressful and, despite being told there is no obligation to donate unused eggs or embryos, couples may feel under pressure to do so.	-1	1	-1
37	You rarely hear about the risks associated with the use of embryonic stem cells: how they can run out of control and form tumours.	0	2	0
38	It is unfair if only those people who can afford it have access to expensive stem cell treatments – they should be available to everyone.	3	0	4
39	The views of the public must be taken into consideration when regulating stem cell research.	2	3	2
40	My initial reaction is that it makes me feel a bit uncomfortable but I can't think of any rational reason why they shouldn't put human DNA into animal cell casings to create stem cells to help cure horrible diseases.	0	-3	-1
41	Life should NEVER be created to grow spare parts for another person.	-1	4	2
42	It's better to donate unused embryos from fertility treatment (IVF) for research than discard them, at least then some good might come of them.	4	-2	-1
43	The rush to experiment with human embryos is premature, driven more by the desire for scientific glory than a clear sense of the most urgent medical needs.	-3	3	-1

44	Science is fuelled by money and the money is controlled by others, so scientists cannot guarantee that the science will not be misused.	0	4	-3
45	It is unreasonable to expect women to go through the discomfort of egg donation altruistically. Doctors and nurses are paid, so why not the women themselves?	-1	-1	3
46	Once the principle of egg donation for research is established it will become harder to prohibit paid egg donation, and the idea of a trade in human eggs is disturbing.	0	1	1