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“It may be that, some ages hence . . . the restoration of grey hairs to juvenility and the renewing of the exhausted marrow may at length be elicited without a miracle.”

Joseph Glanvill,
Founder Member of the Royal Society,
1661AD

Report & Recommendations

November 2005

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Executive Summary

Innovation forms the backbone of the knowledge-based economy and stem cell research represents a substantial opportunity for future innovation in the life sciences. The UK currently enjoys a position of strength in this area, largely because of a supportive regulatory environment. To ensure that the UK remains one of the global leaders in stem cell research, the UK Stem Cell Initiative (UKSCI) was established by the Chancellor, Rt. Hon. Gordon Brown, in his March 2005 Budget [See Annex 1]. UKSCI was charged with developing a ten-year vision and costed strategy for UK stem cell research, for implementation between 2006-2015 [See Annex 2]. Over the last 6 months, UKSCI has consulted widely with academia and the private sector [See Annex 3]. Strengths and weaknesses in UK stem cell research have become apparent and, in this report, we present our recommendations for preserving the former while remedying the latter.

The UKSCI 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.

The development of new stem cell therapies to treat conditions such as Parkinson's disease, diabetes and heart disease is one of the most exciting and captivating aspects of stem cell research. This is a vital and worthy aspiration for UK stem cell research and it remains important for the public and research community to be inspired, energised and driven by this long-term goal. Although it is reasonable to anticipate that some new stem cell therapies will be developed within the next decade, we must also accept that it is probable that this area will take several decades of small incremental advances in science and medicine to come to fruition. In this context, it is worth remembering that conventional pharmaceuticals take between 12-15 years of research and development to bring a product to market.

In order to deliver direct benefit to patients and to the UK economy in the short to medium term, UKSCI foresee that at least some of the UK's investment in stem cell research could also be strategically directed to more conventional areas of medicine. Our vision encompasses the UK being in the vanguard of this area by developing novel stem cell therapies, but also by exploiting stem cell research and technology to develop safer and more effective pharmaceuticals, by illuminating the processes leading to cancer and by continuing to deepen our understanding of basic stem cell biology.

UKSCI has identified five major themes for development, to maintain and increase the momentum of UK stem cell research over the next decade:

- **A Public-Private Consortium in the UK for the Advancement of Stem Cell Technology:** The establishment of consortium of pharmaceutical, healthcare and biotechnology companies with the UK Government to develop stem cells as a resource for discovery in medicine.
- **Extension of the Capacity of UK Stem Cell Research:** Fortification of infrastructure needed to develop stem cell therapy via support for Centres of Excellence, the UK Stem Cell Bank and Cell Therapy Production Units.
- **Consolidation of Research Funding for UK Stem Cell Research:** The development of the UK as a centre for translational and clinical stem cell research, with the help of a public-private partnership between the Government and the *UK Stem Cell Foundation*, along with continuing strategic investment in basic stem cell research via the Research Councils and private funding bodies.
- **Judicious Regulatory Measures to Enable UK Stem Cell Research:** The favourable regulatory climate in the UK for stem cell research should be extended to include clinical applications.

■ **Enhanced Coordination & Communication of UK Stem Cell**

Research: More coordinated activities between Government bodies, research councils and stem cell researchers and increased dialogue with the public over the next decade on stem cell research.

To build upon these themes, UKSCI have made 11 recommendations to act as a strategic guide for public and charity sector investment in UK stem cell research over the next decade [**See Box 1**]. Whilst these recommendations have been designed as a cohesive and comprehensive package of measures, UKSCI believes that the implementation of each one should, by itself, enhance UK stem cell research and, therefore, merits consideration.

Box 1

The 11 Recommendations of the UK Stem Cell Initiative

Recommendation 1: The UK Government should establish a public-private partnership to develop predictive toxicology tools from stem cell lines.

Recommendation 2: *The UK Stem Cell Bank* should be consolidated in new permanent facilities adjacent to its current site and its operational and development costs should be secured for the next decade.

Recommendation 3: The Research Councils should monitor the emergence of Centres of Excellence in stem cell research, designate them as such and strengthen them with core funding.

Recommendation 4: Research Councils and private sector funding bodies should support the development of stem cell therapy production units at UK Centres of Excellence in stem cell research.

Recommendation 5: The Government and Research Councils should strengthen the levels of funding for basic stem cell research over the next decade.

Recommendation 6: The Government should provide funding for clinical and translational stem cell research over the next decade at a level matching that raised by the UK Stem Cell Foundation (UKSCF), up to a maximum of £10M per annum, and administer it via a UKSCF/ Medical Research Council collaboration.

Recommendation 7: The Department of Health must ensure that the promised increase in R&D resources is forthcoming and furthermore, that the full NHS costs of stem cell clinical research trials within the NHS are supported with extra funding from each Spending Review over the next decade to match the increase in research grants and activity.

Recommendation 8: The Government should continue to ensure that regulation of stem cell research is risk-based and proportionate and does not stifle the development of the full range of safe and effective new cell therapies for the benefit of patients. In particular, (i) the Department of Health should establish a specialised research ethics committee for stem cell clinical research; (ii) the Government should clarify the regulatory requirements for the use of animals and animal cells in human stem cell research; & (iii) for the *in vitro* use of embryonic stem cell lines, researchers should be registered with, and submit an annual research summary report to, the UK Stem Cell Bank.

Recommendation 9: The *UK Clinical Research Collaboration* should help to (i) coordinate organisations supporting stem cell research, including all of the relevant Research Councils and the UK Stem Cell Foundation and (ii) ensure that the *National Health Service* is optimally engaged in this area.

Recommendation 10: The Government should allocate additional funding to establish *The UK Stem Cell Cooperative*, to maximise the cross-fertilisation between those involved in the sub-disciplines of UK stem cell research.

Recommendation 11: The Research Councils, charitable funding bodies, and Government Departments should develop a sustained and coordinated programme of public dialogue on stem cell research over the next decade.

We have estimated that our total programme of recommendations over the next ten years has a projected cost range of some £41M to £104M per annum [See Section 5.5]. We have calculated that pre-existing public and private sector funding bodies' investment to support ongoing research efforts in this area is likely to account for approximately £30M per annum over the next decade [See Box 11]. It is vital for the UK to maintain this level of investment in stem cell research and we propose that additional investment is made, ranging from approximately £11M to £74M per annum over the next decade, specifically to supplement funding for the new endeavours recommended in this report.

Although, we recognise that stem cell research is one of many demands on the public purse, our view is that the ultimate health and wealth gains that the UK will enjoy are directly proportional to the proposed additional investment. For example, our strategic approach to support for UK stem cell research is likely to attract further home-grown and overseas researchers and investment from the private sector to the UK. The pharmaceutical and healthcare industries are likely to focus their stem cell research activities in close proximity to the international centres of excellence in stem cell and clinical research, such as those we envisage evolving in the UK over the next decade. In addition, any development of stem cell therapies within NHS structures will considerably strengthen the future capacity of our Health Service to deliver regenerative medicine to the future population of the UK.

We commend the foresight and long-term commitment to stem cell research demonstrated by the UK Government in the establishment of this Initiative. As well as prospective wealth creation within the UK economy, our investment is likely to deliver health benefits to patient populations, both in the UK and globally, long into the future.

Section 3: Challenges facing Stem Cell Therapy

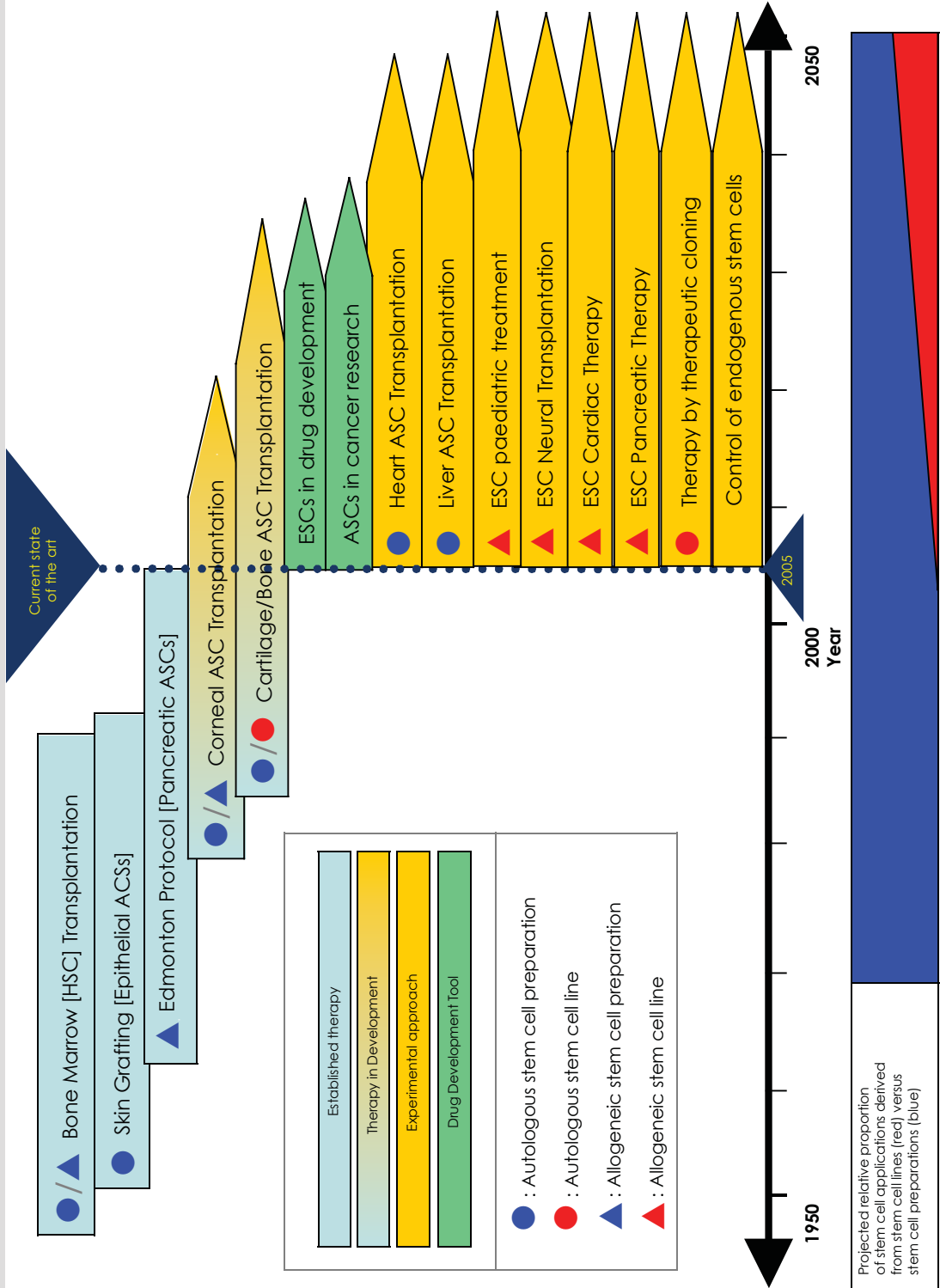
3.1 Lessons from History

The development of future stem cell therapies is likely to mirror many of the historical aspects of pre-existing stem cell therapies [See Boxes 4, 6 & 7]. To that extent, there may be valuable lessons to learn from history. For instance, bone marrow transplantation arose from a desire to convert the basic understanding of immunology, radiation and cancer into clinical benefit for patients. Progress was painstakingly slow, and would not have occurred without experimentation in animals: first in mice, then in dogs. Its success required the parallel development of tissue-matching, materials technology, careful animal experimentation, antibiotics, chemotherapy and the technology of cell separation. Above all, perhaps, the successful development of bone marrow transplantation happened through the dedicated persistence and sustained support for several high-calibre groups of clinical scientists. As with previous stem cell therapies, future stem cell therapies are likely to develop at varying rates and with varying efficiencies [See Box 8], reflecting the breadth of problems encountered for each therapy along the way.

3.2 Classification of Stem Cell Therapy

Therapies using *stem cell preparations* that are not manipulated to any significant degree in the laboratory, such as in some types of corneal transplantation, are likely to develop more quickly. But these are also likely to have restricted clinical utility because the cells are not purified, only defined to a limited extent and consequently less controllable.

Box 8: Timescale for Developments in Stem Cell Research



Legend to Box 8: Timescales for development of Stem Cell Therapies

Research leading to the first clinical applications of stem cells via bone marrow transplantation began before the 1950's. In the subsequent decades, skin grafting, corneal transplantation, cell therapy for the repair of cartilage and the Edmonton protocol for the treatment of diabetes by transplantation of pancreatic cells from cadavers have been developed to successfully treat patients. All exploit the properties of Adult Stem Cells.

Current stem cell treatments are derived, largely, from *stem cell preparations*. As stem cell research develops over the next decades, an increasing proportion of treatments are expected to take advantage of *stem cell lines*, reflecting an increased level of biological control and purity of stem cell therapies.

The current state of the art for stem cell research seeks to: (i) explore adult stem cells in non-homologous settings, such as the use of HSCs in heart repair; (ii) exploit further sources of stem cells, notably Embryonic Stem Cells, for the treatment of paediatric, heart, pancreatic, liver and brain conditions; (iii) use stem cell lines as tools in drug discovery and development; (iv) increase our understanding and treatment of cancer by further studies of endogenous adult stem cells; & (v) generate embryonic stem cells with the same nuclear genetic material to that of the patient using therapeutic cloning techniques, to avoid the potential rejection of cell therapies. Another ambitious goal for the field involves the use of endogenous stem cells, naturally resident in tissues of the human body, to direct the repair of damaged or diseased tissues. In all of the above examples, timescales are unknown and merely indicative.

Section 4: The Global Landscape

4.1 THE INTERNATIONAL CONTEXT

4.1.1 The International Stem Cell Forum

In 2003, the UK's Medical Research Council convened an International Stem Cell Forum, bringing together nine international research agencies that had already shown an interest in working together to further stem cell research. The objectives of the Forum are to develop collaborative research across nations by encouraging the sharing of resources and data and by identifying schemes that would facilitate trans-national collaborations. Overall, the Forum aims to accelerate progress and improve global practice in stem cell research. The Forum, chaired by Professor Colin Blakemore, Chief Executive of the MRC, now consists of research agencies from sixteen countries.

The Forum has taken forward a number of important issues that were identified as being of particular benefit to the advancement of stem cell research. These include:

1. **International Stem Cell Initiative (ISCI):** an international expert working group, led by Professor Peter Andrews (Sheffield University), to draw up globally agreed criteria for characterising stem cell lines derived in different laboratories. This information will form the basis of an International Human ES Cell Registry that will be hosted on the Forum Website. The ISCI held its first meeting in August 2005 to review the initial data being generated by the characterisation project. Some 60 delegates, representing all the 17 participating laboratories from around the world, as well as others with key interests, attended. The meeting was successful in bringing together many of the key participants in this newly emerging field to help shape the future of human ES cell research.

The ISCI represents the first attempt to compare and characterise many of the human ES cell lines derived so far. A second initiative is being developed that will build upon the first characterisation study to address several outstanding problems, such as genetic stability and culture conditions, which are fundamental to the future development of stem cell technology.

- II. **Ethical Landscape Working Group:** One of the ISCF's key objectives is to help facilitate international harmonisation of ethical issues relating to use of stem cells in biomedical research. The Canadian Institute of Health Research set up an ethics sub-committee on behalf of the Forum to identify the ethical issues concerning stem cell research that are emerging throughout the world, and how these might best be addressed.
- III. **IPR Landscape Working Group:** On behalf of the Forum the Australian National Health and Medical Research Council has developed a document about intellectual property (IPR) in stem cell science. This IPR 'landscape' document details the broad criteria for patenting stem cells throughout the world, identifying techniques that may be subject to patenting, highlights those patents already in existence, and explains how countries are attempting to ensure ongoing access to stem cell resources. The information provided will be key in encouraging further research and development world-wide.
- IV. **International Stem Cell Banks:** The UK Stem Cell Bank will be leading on identifying best practice for stem cell banking protocols, including derivation, cryogenics and Good Manufacturing Process, and on how Stem Cell Banks worldwide can best interact and co-operate.

4.1.2 International Competition

The global position of stem cell research is becoming increasingly competitive. Research in the US, China, Singapore and South Korea is proceeding apace and with increasing levels of government support. Recent estimates suggest that Australia, China, Israel, Singapore, South Korea and Sweden are each currently investing between £10M and £90M in this area³. Perhaps most striking is the situation in the United States. Despite federal restrictions on embryonic stem cell research, the

³ Financial Times/Scientific American Special Report on "The Future of Stem Cells". July 2005

National Institute of Health in the USA spent \$517M (£294M) on stem cell research in the fiscal year 2003. Additionally, individual US states are investing substantially in this area. For example, in November 2004, California voted to introduce Proposition 71 into its constitution. This committed \$3B (£1.7B) over the next ten years for stem cell research in California.

The regulatory and funding climates in the most competitive countries in stem cell research are summarised below. Further details on global positions in stem cell research are available at: www.advisorybodies.doh.gov.uk/uksci/global

4.1.2.1 AUSTRALIA

The future of stem cell research in Australia is currently being reviewed as the legislation governing the research is due for renewal. The current legislation, which makes therapeutic cloning illegal, has been in force since 2002 and the review must be completed by 19 December 2005. It is expected that the review will call for therapeutic cloning to be allowed.

Research involving stem cells is managed largely by the Australian Stem Cell Centre (ASCC) based at Monash University in Melbourne. The ASCC has links with many universities around Australia and around the world as well as links with corporate partners. Earlier this year, the Bio21 Institute was opened at the University of Melbourne. Bio21 is the Australian research base for Cygenics Ltd who, through their subsidiary Cordlife Pty Ltd, have moved some of their research from the USA to Australia.

Australian stem cell research has a largely therapeutic focus including research into haematopoiesis; cardiac regeneration and respiratory disease. As therapeutic cloning is illegal, the main technology platforms used are embryonic stem cells, obtained from surplus IVF embryos, adult stem cells, tissue repair and immunology. Funding for stem cell research is mainly from the Australian Government and state governments through various funding schemes with some coming from commercial partners.

The UK and Australia have a long history of scientific collaboration and stem cell research is one area that has been successful. However, there

is increasing scope to attract Australian researchers to the UK and to set up international collaborations, both for research and commercial purposes.

4.1.2.2 CANADA

Canada invests C\$40M (£18.8M) annually on stem cell research. They have established the Canadian Stem Cell Network to co-ordinate research activity and fund major collaborations with a concentration along product development lines. The country has a long history of stem cell research, with current strengths in diabetes, neural research, cancer/blood, stem cell genomics, cardiac, muscle, stem cell bioengineering and ethics. Parliament passed an Act in March 2004 banning human cloning for reproductive or therapeutic purposes. The Assisted Human Reproduction Act allows Canadian researchers to derive new human stem cell lines from embryos left over after fertility treatment. To date, the generation of two human embryonic stem cell lines has been reported. Canadian research is primarily focused on adult stem cell work with some human embryonic stem cell research now underway.

On a global scale, Canadian spend on stem cell research is probably among the top ten nations but it is used more effectively than elsewhere because of its highly coordinated approach.

4.1.2.3 CHINA

The Chinese government has in recent years earmarked stem cell science for special investment, with the aim that China could take a leading role in a high-profile and potentially very important field at a time when Chinese biotechnologists in general are struggling to compete on innovation with their Western counterparts.

The result is a growing patchwork of well-funded teams in China's major cities researching stem cells from adult, fetal and embryonic sources, some connected to large hospitals. Many of these teams are carrying out work of international standing and publishing in Western journals. A recent mission to China from the UK was impressed with what it saw, judging facilities in the labs it visited to be "superb" and government support "excellent".

Overall, Chinese stem cell researchers are more focused on moving the science into the clinic than on understanding the basic mechanisms of stem cell biology. Scientists and clinicians are eager to pursue clinical trials of cell-based therapies and several such trials are now under way to treat brain injury, corneal disease and neurodegenerative illness. This focus reflects the Chinese government's wider approach to science, which is to concentrate funding on applied sciences rather than "blue skies" research.

The country faces fewer moral or public objections to the use of embryonic stem cells than many Western nations. The production of new human embryonic stem cell lines is legal, as is therapeutic cloning. Public opinion seems – as far as one can tell – to be largely positive and focused on the potential medical benefits.

4.1.2.4 CZECH REPUBLIC

The Czech Republic has a strong position in Stem Cell Research with seven 'stabilized' human embryonic stem cell lines derived at the Laboratory of Molecular Medicine in Brno. Molecular biology including stem cell research is one of the seven long-term research priorities of the Czech Republic. Funding from the Ministry of Health and other funding bodies is project oriented and so far, nobody counts expenditure on stem cells separately, so it is not possible at this time to provide accurate and comprehensive figures. A new government Bill regulating stem cell research passed through the government in July 2005 and will go to the Parliament with expected entry into force in July 2006. The legislation is liberal and in many ways mirrors the UK. The UK is perceived as a partner of choice and Czech researchers have many contacts with leading UK experts in stem cell research.

4.1.2.5 DENMARK

With an amendment to the existing Danish Act on Medically Assisted Procreation, it has been possible for Danish scientists to investigate human embryonic stem cells from national sources from September 1, 2003. Only stem cells derived from up to 14-day-old human embryos that are surplus to treatment by In Vitro Fertilisation. Danish embryonic stem cell research must be approved according to the rules of the scientific ethical committee system.

Since September 1 2003, academics have been expecting a strategy and funds for Danish stem cell research but, to date, this has not materialized. A significant part of Danish stem cell research is undertaken and coordinated by The Danish Centre for Stem Cell Research which was established in April 2002 based on nine existing research groups from universities and private research institutes. Denmark seems to be losing ground in stem cell research due to lack of funding, but the existing researchers are well recognized globally and have published several findings of international quality.

4.1.2.6 FRANCE

France permitted research on the embryo and embryonic stem cells for the first time in July 2004, although somatic cell nuclear replacement and the creation of embryos for research remain forbidden. Licensing of embryo research will be the responsibility of a new Agence de Biomedecine. The Agency was established in May 2005, but the secondary legislation establishing its full licensing powers is still being prepared. In the interim, a temporary decree published last October establishes an ad hoc committee to consider applications to import, store and carry out research on embryonic stem cells.

French scientists are now trying to catch up, with a few world class groups in developmental biology and the neuroscience applications of stem cells. However, there is still only a small stem cell research community in France and there is no ring-fenced funding or national strategy. In December 2004, a report from the French Academy of Sciences concluded that the stem cell area required additional funding and clarity of strategy.

4.1.2.7 GERMANY

In June 2002, a majority in the German Bundestag (Lower House) agreed the German Stem Cell Act. This bans in principle the import and use of human embryonic stem cells, the production of which is outlawed in Germany. However, the import of human embryonic stem cells and research projects using human embryonic stem cells will be permitted under certain circumstances: (i) alternative forms of research have been exhausted; (ii) only stem cell lines created before 1 January 2002 are used which have come from surplus embryos created for reproduction; (iii) the aims of the research are worthy and of benefit for

society at large; (iv) applications have been assessed by a high-level ethics committee. There is a licensing authority, Robert Koch Institute in Berlin, to administer the system.

The German Research Foundation (DFG), Germany's Research Councils equivalent, produced an overview of its stem cell funding activities in early August 2005. Between 2000-2007, DFG allocations for stem cell research totalled over €70M (£48M). Of this, €60.37M (£41M) was spent on basic stem cell research between 2000-2005 and €10.1M (£7M) was allocated for stem cell clinical research between 2000-2007.

4.1.2.8 INDIA

The Indian government has realised the potential of this new technology in modern therapeutics and biomedical research. It is developing new policy, increasing funding and strongly recommends that stem cell research and its clinical applications be promoted in the country. Over 15 institutions are involved in stem cell research in India. Ethical guidelines are similar to those of the UK and opportunities exist for collaboration and attracting talent to the UK.

4.1.2.9 ISRAEL

Israel has no specific funding or research policy for stem cell research. The largest sum of money dedicated to stem cell research has been through the Ministry of Industry and Trade (MIT) in establishing a Cell Therapy consortium – with funding around \$15M (£8.3M). Israel is considered a leader in stem cell research with strengths both in embryonic and adult stem cells. Areas of research include blood, bone, liver, pancreatic, heart and nerve cells. Israel has ten stem cell oriented companies. In March 2004, the Israeli Parliament extended until March 2009 the previous 5-year moratorium on genetic intervention for the purpose of human reproductive cloning. The UK is perceived both as having a sound regulatory system and as a major player in stem cell research.

4.1.2.10 JAPAN

The Japanese Government stance towards stem cell research is firmly in line with that of the UK. Two major factors underpin this. Firstly, Japan is keen to maintain its international scientific competitiveness in life sciences, while a nagging insecurity remains that, for all of its economic

and scientific stature, the country did not make a strong enough contribution to the human genome project. Secondly, the Government has a keen eye to the potential healthcare benefits that such research may bring for Japan's rapidly ageing population.

In line with this positive stance, huge investments have been made in national facilities and fundamental research. However, human embryonic stem cell research and clinical work has remained to a large extent held back by the slow development of the regulatory framework.

4.1.2.11 KOREA

The Korean Government has designated the development of Science & Technology as one of its top policy priorities. In 2004, it allocated US\$5B (£2.59B) to support R&D activities - at least US\$2B (£1.03B) is directly funded by government ministries, and industrial R&D contributes the rest.

The Ministry of Science and Technology (MOST) has also set up a National Innovation System, which aims to co-ordinate all the institutions, both public and private, that maximise the creation, application and dissemination of knowledge and information from the research base. As part of this innovation systems approach, MOST has identified '10 next-generation growth engines' - these are the ten key growth industries to be prioritised, including next generation biochemical products.

In parallel with these innovation initiatives is an effort to make science and engineering education and research more closely aligned to the needs of industry. Academic scientists and students will receive increases in remuneration and incentives to collaborate, for example by reforming their curriculum to support the S&T industries.

Korea is in a dynamic phase in regard to stem cell research with a supportive government. President Roh said that his government will not ban scientists from conducting research into stem cells and other bioengineering technologies, despite questions over the ethical issues involved. The Presidential adviser on science and technology, Dr Park Ki-young, also stressed the need for the government to guarantee

freedom for stem cell research. The Ministry of Health and Welfare (MOHW) announced on 12 January 2005 that it officially approved the research led by Dr Hwang Woo-suk in 2004 for the first time since the enactment of the 'Act on Bioethics and Safety'. His research is under the control of strict ethical standards set by the government and research institutes.

In July 2005, the government approved a research project by a local genetic engineering laboratory, the Maria Life Engineering Institute. The researchers will be involved in discovery of ways to develop human stem cells that can contribute to curing such illness as Parkinson's disease, spinal cord paralysis and senile dementia. This is the first case approved by the government for such a specific project on the use of human embryonic stem cells.

4.1.2.12 SINGAPORE

Stem Cell research is a major priority for Singapore and is undertaken in a number of government institutes and private companies, generally with significant government stakes. It has rapidly built up expertise in this area, mainly by importing overseas talent, attracted by state-of-the-art facilities and significant research funding. Priorities include research on diabetes, heart and blood diseases, cancer and neurodegenerative conditions. Singapore has been responsible for a number of significant breakthroughs. Prof. Ariff Bongso of the National University of Singapore was amongst the first to derive embryonic stem cells from human embryos and also to grow human embryonic stem cells on human feeder rather than animal cells. More recently a Singapore company, CellResearch Corporation, has discovered a new source of stem cells from the outer lining of the umbilical cord.

Expenditure on Stem cell research in Singapore is estimated at around S\$40-45m a year (~£13-15m). In July 2005 the British and Singaporean Prime Ministers signed a joint statement on science, engineering and technology which includes an initiative to encourage scientific collaborations and networks.

Stem cell research is identified as a priority area for forging new collaborations between the UK and Singapore. A UK-Singapore stem cell workshop was held in June 2004 at Imperial College and a DTI

GlobalWatch Mission visited Singapore in September 2004. These identified significant opportunities for collaboration with Singapore, in particular using Singapore's state-of-the-art facilities at the Biopolis. Collaborations have already developed or are under discussion resulting from these activities. A second UK-Singapore workshop on stem cell research is planned for 2006. In October 2005 Singapore will host a Keystone Symposium – the first to be held outside North America – on Stem Cells, Senescence and Cancer, dominated by US speakers. In addition to scientific collaboration, potential exists for encouraging Singapore's small but fast-growing biotechnology sector to consider the UK as a research partner and a gateway to Europe. Singapore's ethical and legal environment is similar to that of the UK, where reproductive cloning is banned but research on embryos up to 14 days old is allowed.

4.1.2.13 SWEDEN

Sweden is a world leader in stem cell research, with a regulatory & ethical environment similar to the UK. Increased international competition - and opportunities - are recognised resulting in strong marketing of "Swedish stem cell opportunities" and additional funds for medical (including stem cell) research. Their Research Council "Stem Cell Research Project" amounts to 75m Kr (approx £5.5m) for 2003-2008, but additional funds directed towards individual researchers increase this figure significantly to at least 257.3m Kr (£19m) for 2003-2008. This makes Sweden both a potential collaborator with and competitor for the UK.

4.1.2.14 SWITZERLAND

Switzerland is increasingly active in human embryonic stem cell research, but lack of critical mass in the Swiss research and the commercial spin-out community remains the biggest problem compared with the UK. However, swift passage into law of the pragmatic Swiss Federal Stem Cell Research Act this March and strength in adult stem cell research have opened up a window of opportunity for Switzerland to join international leaders in fundamental research and drug discovery.

There is currently no dedicated Swiss Federal funding programme or mechanism that specifically supports research projects with human

embryonic stem cells. However, since 1990 the Swiss National Science Foundation has funded many individual research projects that investigate adult stem cells. It has also committed budget to such research in other funding programmes.

It is estimated that some £ 2.5 million per annum of Swiss Federal budget is allocated to various projects in adult stem cell research in Switzerland. There is only one research project in Switzerland that works with human embryonic stem cells and this has been receiving a modest annual research budget from the Swiss National Science Foundation.

The Swiss State Secretariat for Education and Research is acutely aware of the opportunity offered by the new legislation now in force and is poised to set up and fund a dedicated new five year National Research Programme on Human Embryonic Stem Cell Research that may be launched as early as 2006. It is estimated that this will receive a new annual budget of about £1M over and above the Federal budget which is in place. Switzerland actively seeks bilateral collaboration with both the UK government and UK research to build the core of this new National Research Programme.

4.1.2.15 UNITED STATES OF AMERICA

The legislative positions of US States regarding stem cell research vary widely, ranging from laws in California, New Jersey, Massachusetts and Connecticut which encourage embryonic stem cell research, including therapeutic cloning, to South Dakota, which strictly forbids research on embryos regardless of the source.

Many states restrict research on aborted fetuses or embryos, but research is often permitted with consent of the patient. Almost half the states also restrict the sale of fetuses or embryos. Louisiana is the only state that specifically prohibits research on IVF embryos. Illinois and Michigan also prohibit research on 'live' embryos. Finally, Arkansas, Iowa, Michigan and North Dakota prohibit research on cloned embryos. Virginia's law also may ban research on cloned embryos, but the statute leaves room for interpretation because 'human being' is not defined and does not specify, whether human being includes blastocysts, embryos or fetuses. California, New Jersey, Massachusetts

and Rhode Island also have human cloning laws, but these laws prohibit cloning only for the purpose of initiating a pregnancy or reproductive cloning, but allow cloning for research. Missouri forbids the use of state funds for reproductive cloning but not for cloning for the purpose of stem cell research, and Nebraska prohibits the use of state funds for embryonic stem cells research.

Although the states are generally behaving in a partisan Republican/Democrat manner when it comes to stem cell research, there are some controversies, such as in Massachusetts where the Republican governor had fought with and lost to Democratic legislators over the issue.

A number of states have pledged funding for stem cell research. California is leading these efforts and has pledged \$3B (£1.7B) during the next decade for stem cell research. Other states such as Wisconsin have committed \$375M (£213M), New Jersey \$380M (£216M) and Illinois' comptroller has recommended that his state commit \$1B (£568M). While states are trying to gather enough resources to recruit lead scientists in the field it remains to be seen if a brain drain to well funded states will occur and to what extent leading researchers and science will follow the money.

4.2 STEM CELL RESEARCH IN THE UK

In March 2005, The UK Stem Cell Initiative was established by the Chancellor, Rt. Hon. Gordon Brown, to produce a vision and strategy to keep the UK at the leading edge of global stem cell research over the next decade.

To achieve this aim, it is important to recognise that UK stem cell research currently has a number of strengths which need to be preserved and a number of weaknesses which need to be remedied. The weaknesses are likely to become increasingly evident as the applied benefits from stem cell research emerge. In order to highlight these elements, we have carried out a SWOT analysis for UK stem cell research [**See Box 9**].

Box 9 SWOT analysis of UK Stem Cell Research

Strengths

- Supportive and consistent Government position
- Enabling regulation for embryonic stem cell research
- Favourable ethical environment & public support
- World-class academic researchers in developmental and reproductive biology
- Strong climate of innovation in UK
- UK Stem Cell Bank
- National Blood Service
- Estimated £30M per annum investment in UK stem cell research from public and charity sector funding bodies
- Strong bio-processing initiative
- Strong clinical trials base and UKCRC

Weaknesses

- Gaps in UK funding for translational research
- Unknown business model & return on investment
- Lack of involvement by big pharmaceutical companies
- Lack of venture capital investment
- Lack of regulatory clarity for clinical use of stem cell therapies
- Lack of central co-ordinated strategy leading to “cottage industry” approach
- Smaller science base than US
- History of innovations being lost to the US for commercialisation phase
- Lack of clarity on Intellectual Property and Licensing Issues

Opportunities

- World leadership in embryonic stem cell therapies
- Enhanced drug development & cancer research
- Use NHS to drive clinical translation
- Redirect UK researchers from developmental biology to stem cell research
- Public investment matched by private funding
- Attract foreign skills as international hub
- Drive international agenda
- Attract international inward investment
- Develop international alliances

Threats

- Lack of infrastructure impedes clinical translation
- ‘Brain-drain’ to US & Far East
- Intellectual Property captured in US & Far East
- UK biotechnology sector weakens
- EU moves to limit stem cell research
- Clinical trial adverse events unravels public support
- NHS has to import expensive stem cell treatments for care of aging population

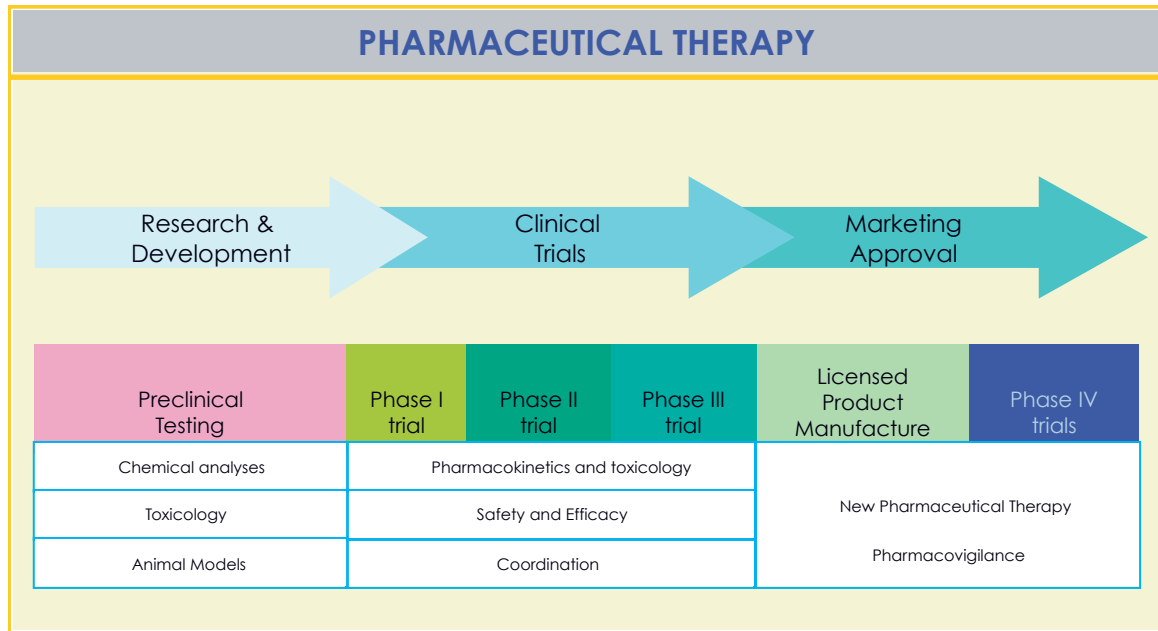
Section 5: Investment Strategy

5.1 RESEARCH CAPACITY

The requirements for the development of stem cell therapies for regenerative medicine are very different from those of more traditional pharmaceutical medicines. This is because any stem cell therapy contains living material and needs to be manufactured, processed and stored in entirely different ways to pharmaceuticals. In the pharmaceutical industry, medicines have been successfully developed over a number of decades through a well-established 'pipeline', which allows the safety and efficacy of drugs to be evaluated at each stage of development [**See Box 14**]. Because this is a tried and trusted approach to drug discovery, the research infrastructure needed to support this pipeline is either already in existence or is readily supported by investment from industry.

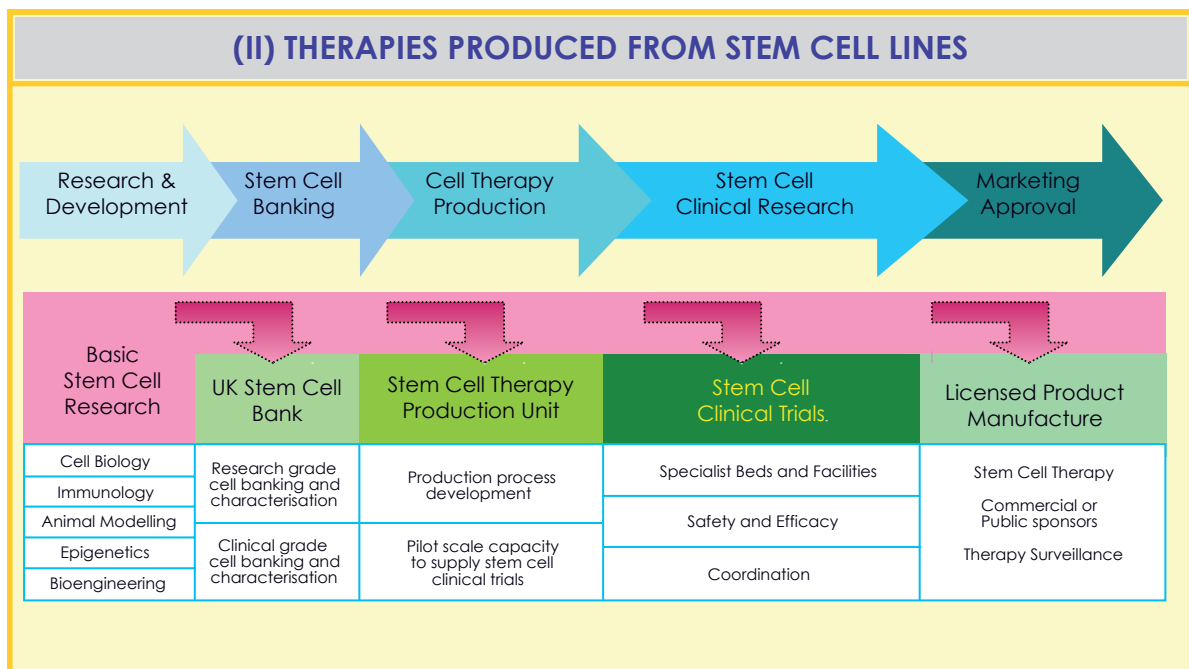
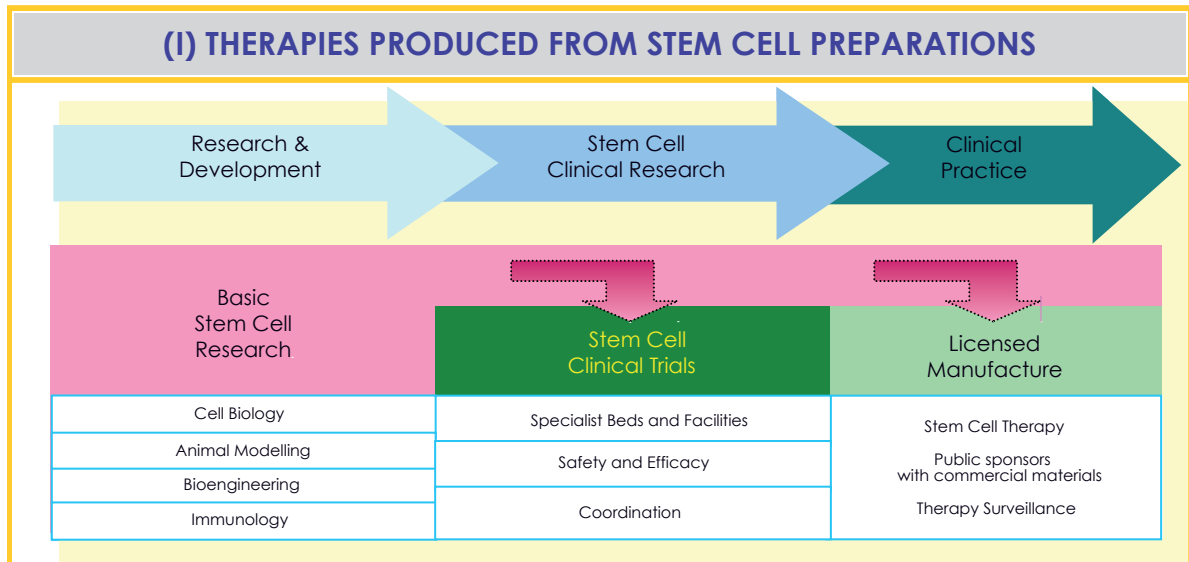
Because stem cell therapy is a less developed aspect of medicine than pharmaceutical discovery, there is no established pipeline for the development of stem cell therapies. However, each of the steps required in the development of novel stem cell therapies can be predicted. UKSCI foresees the development of a range of stem cell therapies in the UK via the pipelines of **Box 15**.

Box 14 The Drug Development Pipeline



Compounds are tested in the laboratory during the research and development stages. Successful lead candidate drugs are next tested on patients in clinical trials. In Phase I trials, the safety and pharmacological activity of compounds is examined in a small number of people. If proven safe and tolerable, drugs are tested on a greater number of patients in Phase II trials. If the drug shows both efficacy and continued safety, it then passes to Phase III trials, involving a large number of patients. The results from the Phase III trials are used to determine whether the drug can receive a licence from the regulatory agency, which would allow it to be marketed and prescribed by doctors. Marketed drugs continue to be monitored for safety in both the general patient population and in specific 'post-marketing' studies, known as Phase IV trials.

Box 15 Stem Cell Therapy Development Pipelines



See legend on next page

Legend to Box 15: Stem Cell Therapy Development Pipelines

Stem cell therapies can be produced from two sources: stem cell preparations, Box 15(I), or stem cell lines, Box 15(II).

Stem cell preparations are isolated from a donor or the patient themselves, as in bone marrow transplantation. Stem cells may sometimes be purified from the preparation before being transplanted into the patient. By contrast, stem cell lines are generated from stem cells that have been derived from donors but grown to homogeneity in laboratory culture. Lines are banked as pure frozen stocks. They can later be expanded to large numbers in the laboratory, differentiated into the therapeutic cell type and transplanted into patients.

During the Research & Development stages, innovations from Basic stem cell research (pink) play a vital role in identifying potentially relevant clinical targets. This area impacts upon all stages of the development of stem cell therapies (indicated by purple arrows). All stem cell therapy requires an understanding of cell biology, bioprocessing and studies in animal models. Allogeneic therapies, as either stem cell preparations or stem cell lines, require knowledge of immune system responses to the transplanted cells.

Stem Cell Banking stages are required to maintain the security and quality of supply of stem cell lines. The UK Stem Cell Bank ensures that cell lines have suitable ethical provenance, are screened for relevant infectious agents and characterised to an appropriate degree. Cell lines can be produced to sufficient quality for clinical or laboratory research applications. At Cell Therapy Production stages, Stem Cell Therapy Production Units develop processes to grow stem cells to a volume which can supply the demand for the large numbers of cells to treat patients in clinical trials.

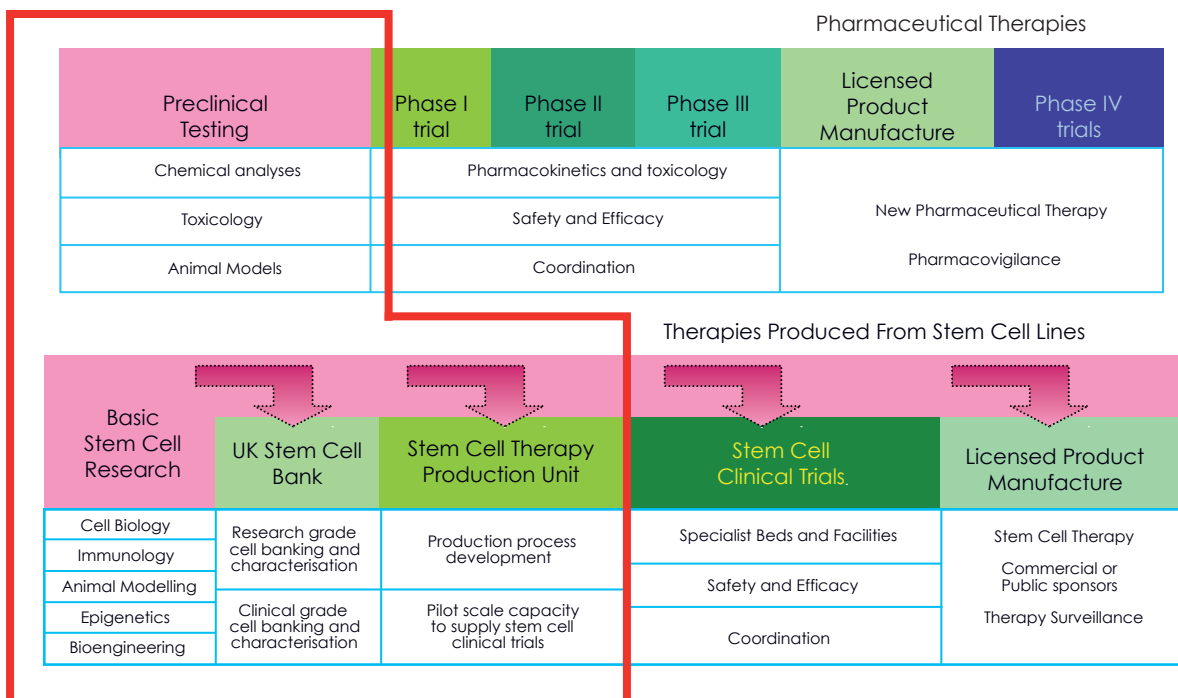
At Stem Cell Clinical Research stages, the safety and efficacy of stem cell therapies derived from both stem cell lines and stem cell preparations are assessed in Stem Cell Clinical Trials. Trials require specialist beds and facilities to monitor the response of patients to treatment. Clinical research requires a considerable degree of coordination, both in managing individual trials and in strategic analyses of funding areas for grant-awarding agencies and policy-makers.

Stem cell preparations tend to have little commercial value and develop as treatments from publicly-sponsored research. As their use reaches Clinical Practice, devices that facilitate the use of these therapies are manufactured under license from the commercial sector. By contrast, therapies developed from stem cell lines have commercial value in themselves and are manufactured as products under license, once they have received Marketing Approval from regulatory agencies. New stem cell therapies are kept under surveillance after marketing approval, to detect any adverse reactions that were not observed during clinical research stages.

Another potential area of specialisation for the consortium could be the development of placental or umbilical cord stem cell banking services and therapies. However, within the time constraints of this report, we have been unable to examine the case for this in sufficient detail.

Perhaps most importantly a public-private consortium focusing on the understanding required for the use of stem cells in predictive toxicology would help develop technology to improve the safety and range of conventional pharmaceuticals and expedite the development of stem cell therapies for regenerative medicine. This would contribute to stem cells having a positive impact on patient's health sooner rather than later.

Recommendation 1: The UK Government should establish a public-private partnership to develop predictive toxicology tools from stem cell lines.



Projected Cost Range of UKSCI Recommendation 1: £16.4 – 31.3M

LOW TRAJECTORY (£M):

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Management costs ¹	0.2	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
Costs of research ²	0.5	1	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Cost per year	0.7	1.3	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8

HIGH TRAJECTORY (£M):

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Management costs ³	0.5	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7
Costs of research ²	0.5	1	2	3	3	3	3	3	3	3
Cost per year	1.0	1.7	2.7	3.7	3.7	3.7	3.7	3.7	3.7	3.7

¹Based on recruitment of a Chief Executive to develop commercial partners, business planning, research portfolio development planning and scientific advisory board, along with additional funding for administrative assistance and office space. Further funding for management team to come from commercial partners.

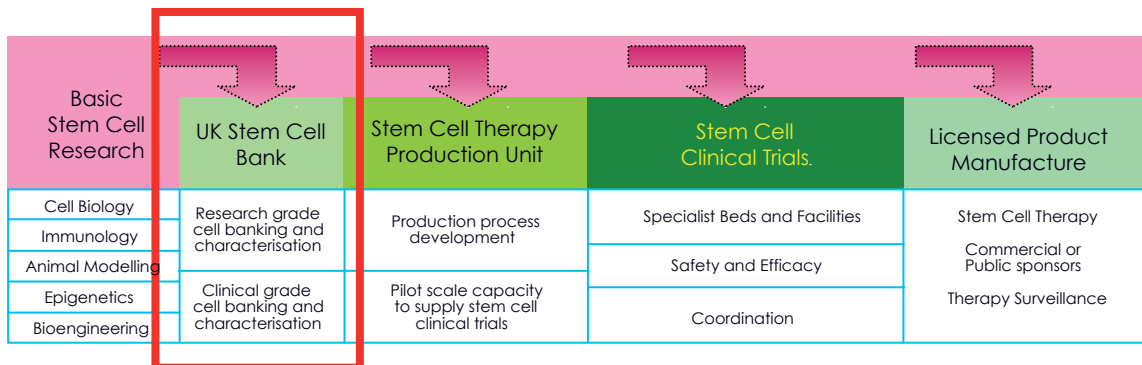
²Figures represent seed Government funding to commission research. Further substantial investment to fund research to be contributed from commercial partners. Costings profiled for each research project to span three years.

³Includes salaries for Chief Executive, Finance Officer, Legal Officer, administrative assistance and office space.

5.1.2 Stem Cell Banking

The UK Stem Cell Bank is co-funded by the BBSRC and MRC. It plays a crucial role in ensuring the ethical provenance, quality and secure supply of stem cell lines in the UK. The Bank also contributes to the development of stem cell technology in general and to a stem cell therapy development programme by providing centrally-based expertise in the handling and storage of stem cell lines. The Stem Cell Bank is currently synonymous with embryonic stem cell lines. In the future, it should ensure that it develops expertise in the handling and storage of stem cell lines from all sources, including adult stem cells. The Bank should also ensure that it can accommodate the anticipated increase in requests for withdrawals of stem cell lines over the next decade. In addition to this anticipated increase in transactions, the Bank should become the international centre in the development of stem cell banking protocols, processes and techniques, such as in cryogenics, infection control and Good Manufacturing Practice (GMP).

Recommendation 2: The UK Stem Cell Bank should be consolidated in new permanent facilities adjacent to its current site and its operational and development costs should be secured for the next decade.



Projected Cost Range of UKSCI Recommendation 2: £17.0 – 20.8M

LOW TRAJECTORY (£M):

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Capital building costs ¹	3.4	0	0	0	0	0	0	0	0	0
Operational costs ²	1	1	1	1.1	1.1	1.1	1.2	1.2	1.2	1.2
Development costs ³	0.2	0.2	0.2	0.2	0.2	0.3	0.3	0.3	0.3	0.3
Cost per year	4.6	1.2	1.2	1.3	1.3	1.4	1.5	1.5	1.5	1.5

HIGH TRAJECTORY (£M):

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Capital building costs ¹	4.5	0	0	0	0	0	0	0	0	0
Operational costs ²	1	1	1	1.2	1.2	1.2	1.3	1.3	1.3	1.3
Development costs ³	0.4	0.4	0.4	0.4	0.4	0.5	0.5	0.5	0.5	0.5
Cost per year	5.9	1.4	1.4	1.6	1.6	1.7	1.8	1.8	1.8	1.8

¹Single cost expenditure in 2006 to finance permanent facilities for UK Stem Cell Bank.

²Maintenance and supply of stem cell lines, salary support, and administration costs, profiled to increase with demand by 2009.

³Costs for the development of techniques and protocols in cryogenics, infection control and GMP, profiles to increase in cost by 2011.

5.1.3 Centres of Excellence

The discussions we had as part of this review impressed upon us the multidisciplinary nature of stem cell research, the long-term nature of the endeavour and the relatively small cadre of scientific, clinical and technical staff involved in the UK. Moreover, there is in stem cell research a requirement for somewhat repetitive development and maintenance work for which it is difficult to obtain grants when proposals are in competition with those incorporating novel, hypothesis driven science. Accordingly, high quality, internationally competitive research in the UK will develop in locations that make a, strategic, long-term commitment to such research and fund it with contributions from all possible sources. We believe Centres of Excellence in UK stem cell research will evolve in the coming years and play vital roles as:

- locations within the UK where the best researchers can interact and share their ideas, talents and energy;
- dedicated and specialised facilities for multiple aspects of stem cell research;
- hothouses for the specialised training needed to expand the cadre of UK stem cell researchers; and
- infrastructure to attract internationally acclaimed stem cell research groups to the UK.

Central to the rationale for Centres of Excellence is the recognition that there is a considerable danger that a shortage of human resources at all levels will limit the overall capacity for growth of UK stem cell research over the next decade. In particular, it will be critical to ensure that sufficient training opportunities exist for post-graduate and post-doctoral researchers so that they can be attracted to long-term careers in this area. Centres of Excellence should provide such opportunities. In addition, we note that there is a large body of internationally-acclaimed researchers working on developmental and reproductive biology in the UK. In order to increase the number of stem cell researchers in the UK it should be possible to entice some of these into stem cell research. Again, Centres of Excellence should provide the locations and facilities capable of achieving this.

Finally, in terms of existing UK stem cell researchers, it is vital that every effort is made to avoid the loss of these key personnel. One of the principle threats to UK stem cell research comes from international competition. With very substantial levels of funding in California, Singapore, China and South Korea, there are concerns that UK researchers, particularly younger ones, will be attracted to working in these overseas economies. The resultant loss of skilled personnel and intellectual property rights could adversely affect the entire UK biotechnology sector. Encouragingly, the UK is already perceived by both researchers in the UK and abroad as providing a first class regulatory environment for stem cell research. However, we are aware of one recent instance of a key scientist moving abroad in response to substantial funding being made available elsewhere. Providing core funding for Centres of Excellence should help combat this.

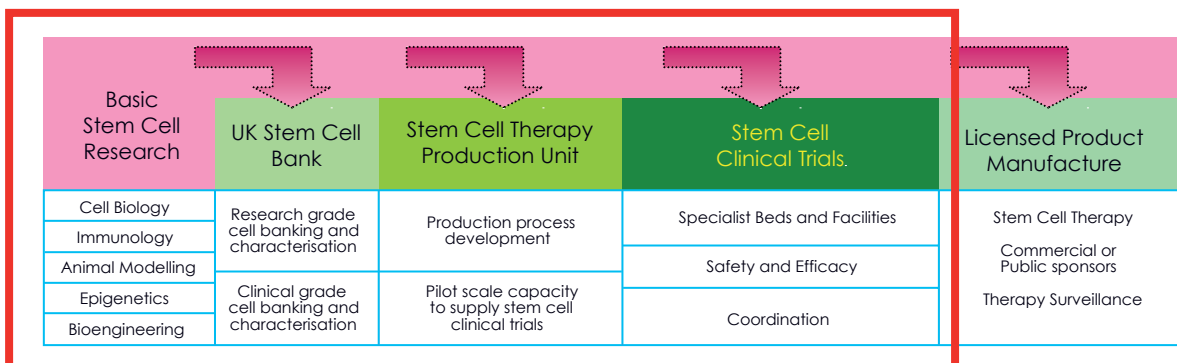
In March 2005, the Academic Subcommittee of the Modernising Medical Careers and UK Clinical Research Collaboration published a report aimed at improving the academic career prospects for medically-qualified researchers in the UK. The committee, chaired by Dr Mark Walport, Director of the Wellcome Trust, set out a clear training pathway for doctors wishing to pursue academic careers. The report's recommendations were supported by £2.5M committed by the Department of Health to pilot the establishment of an integrated academic training programme as a foundation for the academic clinicians of the future. Drawing on the lessons from the Walport report, there is a critical need for contributions from clinical scientists in the early stages of the development of stem cell therapies within the UK research base. Based on their clinical knowledge of the therapeutic area, medically-qualified researchers are best placed to optimise the design and development of new treatments for patients. The Department of Health should ensure full implementation of the Walport report and funding bodies should prioritise the recruitment of medically-qualified researchers, to be embedded within basic and translational groups in the UK Centres of Excellence in stem cell research.

During the preparation of this review, we have become aware of the possibility of a number of top international scientists in stem cell research moving to the UK. We commend the efforts of Universities and funding bodies to enable these recruitments to occur. Whilst we

recognise that some funds for recruitment are available, for example, via allocations from the Higher Education Funding Council for England (HEFCE), the MRC's Strategic Appointments Awards or the Wellcome Trust's Principal Research Fellowship Scheme, there is a limit to how far this can be achieved without additional resources. Nevertheless, it is of critical importance to be able to grasp these opportunities during the relatively short time they are available. They provide an additional means of increasing the numbers of scientists involved in stem cell research in the UK. Such researchers are only likely to be attracted to and thrive in Centres of Excellence.

It will be important for the Research Councils to resource the development of such Centres of Excellence if we are to foster an environment in the UK that is conducive for the development of ideas from "bench to bedside". Centres of Excellence should be monitored jointly by the relevant Research Councils, so that excellence in the necessary biological, engineering, social science and the arts and humanities can be recognised. Key to their success will be the availability of sufficient and adequate NHS support for clinical studies. Therefore, additional resources should be requested in Spending Reviews, as necessary.

Recommendation 3: The Research Councils should monitor the emergence of Centres of Excellence in stem cell research, designate them as such and strengthen them with core funding.



Projected Cost Range of UKSCI Recommendation 3: £36 – 70M

LOW TRAJECTORY (£M):

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Centres Of Excellence ¹	2	2	2	2	4	4	4	4	4	4
Recruitment of internationally-acclaimed research groups ²	2	2	0	0	0	0	0	0	0	0
Cost per year	4	4	2	2	4	4	4	4	4	4

HIGH TRAJECTORY (£M):

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Centres Of Excellence ³	2	2	4	4	6	6	8	8	10	10
Recruitment of internationally-acclaimed research groups ⁴	2	2	2	0	0	2	0	0	2	0
Cost per year	4	4	6	4	6	8	8	8	12	10

¹Based on two rounds of designation of UK Centres of Excellence in stem cell research in 2006 & one in 2010.

²Based on the recruitment of two internationally-acclaimed research groups, one in 2006 & one in 2007.

³Based on five rounds of designation of UK Centres of Excellence in stem cell research in 2006, 2008, 2010, 2012 & 2014.

⁴Based on the recruitment of five internationally-acclaimed research groups, one each in 2006, 2007, 2008, 2011 & 2014.

5.1.4 Cell Therapy Production Units

Currently, there are a number of infrastructure components from the stem cell therapy development pipeline, which are missing from, or are limited in, the UK. Therapies involving stem cell lines will require facilities to allow researchers to develop processes to produce clinical grade batches of cells for use in clinical trials. Our vision for UK stem cell research is to include the development of therapies for regenerative medicine, so we must ensure that the infrastructure for every component of this envisaged pipeline is in place.

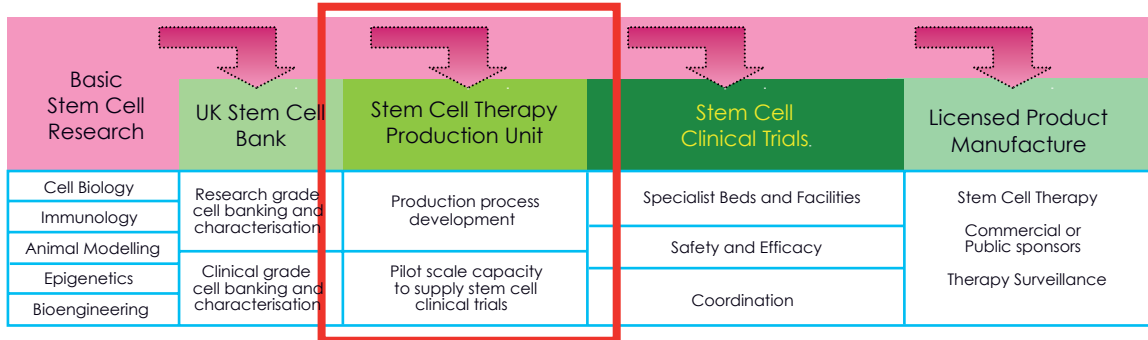
The infrastructure to produce large volumes of cells for clinical trials is essential to the successful development of stem cell research. It will eventually be important to develop multiple national facilities at centres of excellence to maximise the potential for demonstrating proof-of-concept in any particular stem cell therapy.

Such facilities should provide a vital, and currently missing, infrastructural component to a number of research centres and will allow ideas for new treatments to be developed from “bench to bedside.” The facilities should be capable of developing processes required to produce clinical grade material derived from both adult and embryonic sources of stem cells and producing pilot-scale clinical grade material for use in clinical trials.

It will be essential to ensure that these facilities are staffed appropriately or their use will be extremely limited. These facilities will act as training centres in the UK for the development of the technical skills base in cell therapy. The availability of long term funding for posts in these facilities will attract technical staff to careers in cell-based therapy.

Until allogeneic stem cell therapy is applied to a range of illnesses in patients, UKSCI believes that the commercial sector is unlikely to fill these infrastructural gaps in the pipeline by investment. It therefore falls to Government, the Research Councils, the National Blood Service and other funding bodies to build this capacity within the UK.

Recommendation 4: Research Councils and funding bodies should support the development of stem cell therapy production units at UK Centres of Excellence in stem cell research.



Projected Cost Range of UKSCI Recommendation 4: £12.2 – 43.4M

LOW TRAJECTORY (£M):

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Capital building costs ¹	2	0	0	0	0	0	0	0	0	0
Operational costs ²	0	1	1	1	1.2	1.2	1.2	1.2	1.2	1.2
Cost per year	2	1	1	1	1.2	1.2	1.2	1.2	1.2	1.2

HIGH TRAJECTORY (£M):

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Capital building costs ³	3	0	3	0	3	0	3	0	3	0
Operational costs ²	0	1	1	2	2.2	3.2	3.4	4.4	4.6	5.6
Cost per year	3	1	4	2	5.2	3.2	6.4	4.4	8.6	5.6

¹Based on the development of one Cell Therapy Production Unit in the UK in 2006.

²Cell Therapy Production Units' operational costs profiled to increase four years after establishment by 20%.

³Based on the development of five Cell Therapy Production Unit in the UK between 2006-2015.

5.2 RESEARCH SUPPORT

UK stem cell research receives considerable financial support from a broad spectrum of funding agencies. In relative terms, current levels of funding for UK stem cell research are competitive internationally, with the exception of the significant federal and state funding in the USA [See Section 4]. Over the next decade, the anticipated expansion in the UK stem cell research base will increase the demand for funding in this area in the UK.

5.2.1 Basic stem cell research

Funding bodies believe that the current resources have funded high-quality proposals for stem cell research and that this has been effective in initiating research in this area. We have estimated that the Research Councils are currently spending £15M per annum on this [See Box 11]. However, the overall funding of the science base is restricted and stem cell research requires continuing long term investment and is relatively expensive.

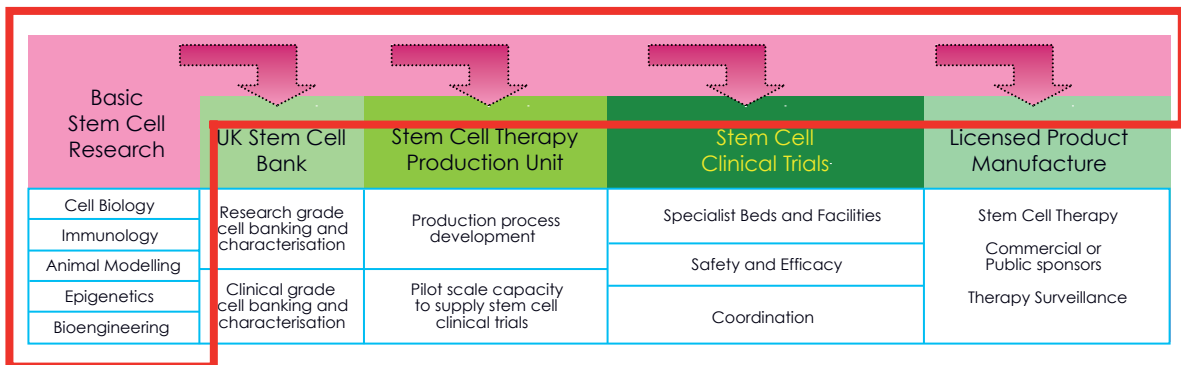
Basic stem cell research will contribute to all stages of stem cell technology and therapy development. It will form the bedrock for any innovation, from which crucial intellectual property rights can be established. High priority should, therefore, be given to integrated research programmes that are interdisciplinary and directed towards the conversion of basic stem cell research into clinical applications.

If we are committed to making a contribution to the field in the international context, we must accept the need to fund basic stem cell research to a significant degree. If the UK Stem Cell Bank is to be fully resourced, internationally acclaimed researchers are to be recruited to the UK, Centres of Excellence are to be supported and the benefits of stem cell therapies are to be realised, then more resources for UK stem cell research through conventional channels will be required. Otherwise, other parts of the UK science base will suffer.

While we cannot expect to invest the levels of funding in stem cell research that are being proposed by California, \$3B over ten years, the UK Government should be prepared to commit to respond to Spending

Review bids for basic stem cell research. It is impossible to predict how much might be required, but for the purposes of our indicative costings, we estimate that a profiled increase of £5 - 21M per annum will be required over the next decade.

Recommendation 5: The Government and Research Councils should strengthen the levels of funding for basic stem cell research over the next decade.



Projected Cost Range of UKSCI Recommendation 5: £200 – 272M

LOW TRAJECTORY (£M):

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Existing commitment to Basic Stem Cell Research ¹	15	15	15	15	15	15	15	15	15	15
New Funding for Basic Stem Cell Research ²	5	5	5	5	5	5	5	5	5	5
Cost per year	20	20	20	20	20	20	20	20	20	20

HIGH TRAJECTORY (£M):

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Existing commitment to Basic Stem Cell Research ¹	15	15	15	15	15	15	15	15	15	15
New Funding for Basic Stem Cell Research ³	5	5	7	9	11	13	15	17	19	21
Cost per year	20	20	22	24	26	28	30	32	34	36

¹Based on the estimated spending by Research Councils on stem cell research in 2005 [See Box 11].

²Based on additional spending by Research Councils on stem cell research of £5M per annum between 2006 & 2015.

³Based on spending by Research Councils on stem cell research increasing from £5M per annum in 2006 and 2007 and, profiled to increase to £21M per annum by 2015

5.2.2 Translational & Clinical Research

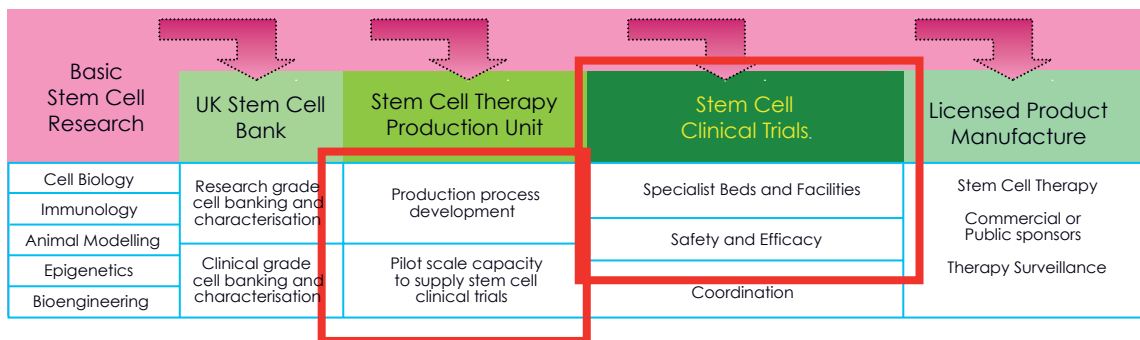
The majority of translational research in the next five years is likely to involve adult stem cells. It is expected that there will be an increasing number of embryonic stem cell applications in the subsequent years. The expertise gained earlier from the development of adult stem cell therapies will expedite the development of therapies involving embryonic stem cells. It is therefore essential that the UK is supportive of early clinical stem cell research trials, provided they are of sufficient quality. This will help to develop our breath of expertise and knowledge of clinical aspects of stem cell research.

The UK Stem Cell Foundation (UKSCF) has been established specifically to fund translational and clinical stem cell research in the UK and seeks to raise substantial funds (up to £10M per annum) from private donations in order to promote this research. The Foundation recognises the emerging potential of stem cell research to create health benefits in the UK and is determined that these opportunities should not be lost. It has suggested that the Government matches the private money raised pound-for-pound.

Consideration should be given to this proposal, as it would effectively halve the cost to the public purse of funding such translational and clinical research in the UK. The research proposed must be of high quality and to ensure this, the UKSCF and the MRC are jointly developing specific selection criteria and a combined review process for the funding of translational stem cell research proposals. If UKSCF/MRC successfully develop this joint process, the Government could administer this new funding via a UKSCF/MRC collaboration. Public money would be allocated to the MRC for the specific purpose of matching UKSCF funding for translational and clinical stem cell research projects.

Should such a partnership prove possible, then it would undoubtedly contribute to the development of stem cell therapy in the UK by providing much needed support for research aimed at clinical application within two years.

Recommendation 6: The Government should provide funding for clinical and translational stem cell research over the next decade at a level matching that raised by the UK Stem Cell Foundation (UKSCF), up to a maximum of £10M per annum, and administer it via a UKSCF/Medical Research Council collaboration.



Projected Cost Range of UKSCI Recommendation 6: £83 – 87M

LOW TRAJECTORY (£M):

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
UK Stem Cell Foundation ¹	2	5	7	9	10	10	10	10	10	10
Cost per year	2	5	7	9	10	10	10	10	10	10

HIGH TRAJECTORY (£M):

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
UK Stem Cell Foundation ²	2	5	10	10	10	10	10	10	10	10
Cost per year	2	5	10	10	10	10	10	10	10	10

¹Based on a profiled increase in fund-raising by the UKSCF, that requires matching funding of £10M each year by 2010.

²Based on the UKSCF raising funds of £10M (or over) each year from 2006 to 2015.

The new allocation of money to the UKSCF raises a second issue with respect to public funding for translational and clinical stem cell research. These studies are likely to fail if the NHS is unable to support the additional costs of these experimental therapies. Therefore, It will be critical to increase funding of NHS R&D.

As well as the 'Direct Research Costs', the cost of clinical research in the NHS is composed of 'Service Support Costs', which are the extra costs associated with care and monitoring of patients in clinical trials, and the 'Excess Treatment Costs', which are the costs of providing the experimental treatment above those of the standard regimen. Retrospective analyses of clinical research in the NHS reveals that Service Support Costs and Excess Treatment Costs are each equivalent to the Direct Research Costs. That is, the cost of clinical research in the NHS is twice that of the Direct Research Costs.

In 2004, a major increase in the overall NHS R&D allocation was made but, subsequently, much of this increase has been delayed. Should the Government wish to support stem cell clinical research, then the new NHS R&D resource previously promised will have to be restored and additional money to meet the full NHS costs of stem cell trials will need to be made available. We estimate this latter requirement will grow to £32M per annum over the next decade.

Recommendation 7: The Department of Health must ensure that the promised increase in R&D resources is forthcoming and furthermore, that the full NHS costs of stem cell clinical research trials within the NHS are supported with extra funding from each Spending Review over the next decade to match the increase in research grants and activity.

Basic Stem Cell Research	UK Stem Cell Bank	Stem Cell Therapy Production Unit	Stem Cell Clinical Trials	Licensed Product Manufacture
Cell Biology	Research grade cell banking and characterisation	Production process development	Specialist Beds and Facilities	Stem Cell Therapy Commercial or Public sponsors Therapy Surveillance
Immunology			Safety and Efficacy	
Animal Modelling	Clinical grade cell banking and characterisation	Pilot scale capacity to supply stem cell clinical trials	Coordination	
Epigenetics				
Bioengineering				

¹Projected Cost Range of UKSCI Recommendation 7: £265.6 – 278.4M

LOW TRAJECTORY (£M):

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Full NHS Cost ²	6.4	16	22.4	28.8	32	32	32	32	32	32
Cost per year	6.4	16	22.4	28.8	32	32	32	32	32	32

HIGH TRAJECTORY (£M):

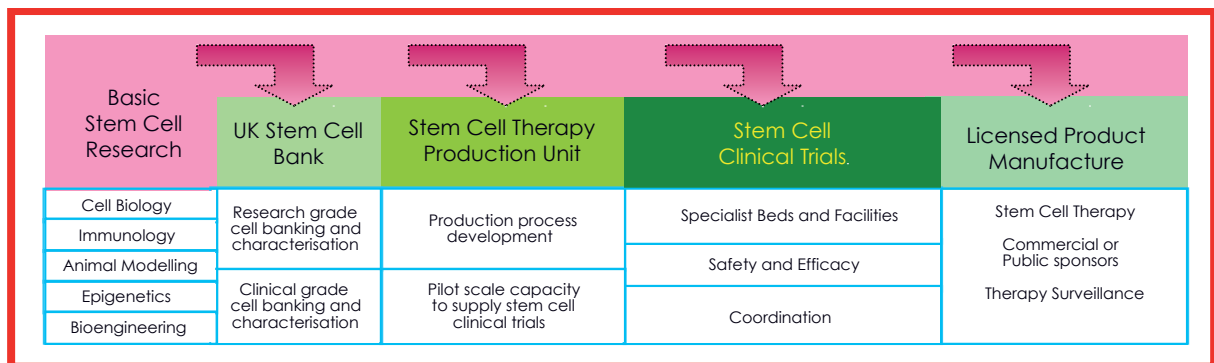
Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Full NHS Cost ³	6.4	16	32	32	32	32	32	32	32	32
Cost per year	6.4	16	32	32	32	32	32	32	32	32

¹The Full NHS Cost of clinical research is composed of Service Support Costs and Excess Treatment Costs, both of which are the same as Direct Research Costs. Figures are based on funding raised by UKSCF being equivalently matched by public money, as in Recommendation 6. UKSCF estimate that 80% of their funding will support of clinical trials in the NHS. Therefore, the cost per year has been calculated according to the formula: **[Full NHS Cost]= 2 X [0.8 X (Funding raised by UKSCF + Matching public funding to UKSCF)]**.

²Based on a profiled increase in fund-raising by the UKSCF that requires matching funding of £10M each year by 2010.

³Based on a profiled increase in fund-raising by the UKSCF that requires matching funding of £10M each year by 2008.

Recommendation 8: The Government should continue to ensure that regulation of stem cell research is risk-based and proportionate and does not stifle the development of the full range of safe and effective new cell therapies for the benefit of patients. In particular, (i) the Department of Health should establish a specialised research ethics committee for stem cell clinical research; (ii) the Government should clarify the regulatory requirements for the use of animals and animal cells in human stem cell research; & (iii) for the *in vitro* use of embryonic stem cell lines, researchers should be registered with, and submit an annual research summary report to, the UK Stem Cell Bank.



Projected Cost of UKSCI Recommendation 8: £5M

COST (£M):

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Stem Cell Therapy Specialised Ethics Committee expenditure ¹	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Cost per year	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5

¹Based on figures from similar Government Scientific Advisory Committees in the life sciences.

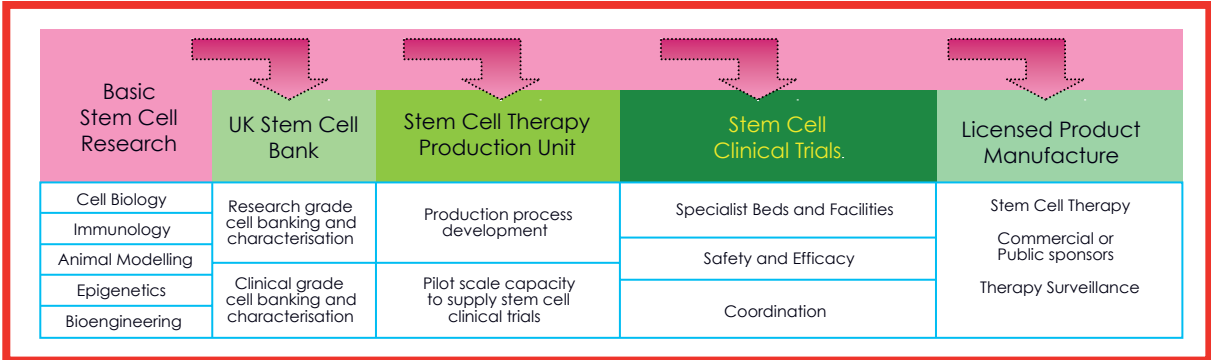
5.4 COORDINATION & COMMUNICATION

5.4.1 Strategic Coordination

As outlined in **Section 4**, a number of countries offer strengths in stem cell research which are complementary to those of the UK. The Government currently has a number of disparate programmes that promote UK stem cell research and gather information on research globally, such as the DTI *Globalwatch* missions, *UK Trade and Investment* and the *Science and Innovation Network* of the Foreign & Commonwealth Office. Global strategic alliances between the UK and other countries in areas of mutual interest in stem cell research should be developed in a coordinated fashion, based on input from all relevant Government Departments and the Research Councils. The Department of Health, Department of Trade & Industry, Foreign & Commonwealth Office, Research Councils and other relevant Government bodies should coordinate activities to consolidate the global position of UK stem cell research, including via the development of strategic alliances with other countries that have complementary interests to the UK.

Because of the multidisciplinary nature of stem cell research, the Research Councils should continue to work closely together to develop cross-functional research programmes, such as in bioengineering. It continues to be essential for the Research Councils to coordinate their activities if we are to see maximum value for our investment in this area. One of the work streams of the UK Clinical Research Collaboration involves experimental medicine. It would seem a natural progression for the UKCRC to coordinate the efforts of the Research Councils and charitable funding bodies that support stem cell research.

Recommendation 9: The UK Clinical Research Collaboration should help to (i) coordinate organisations supporting stem cell research, including all of the relevant Research Councils and the UK Stem Cell Foundation and (ii) ensure that the National Health Service is optimally engaged in this area.



Projected Cost of UKSCI Recommendation 9: £1M

COST (£M):

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
UKCRC expenditure ¹	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Cost per year	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1

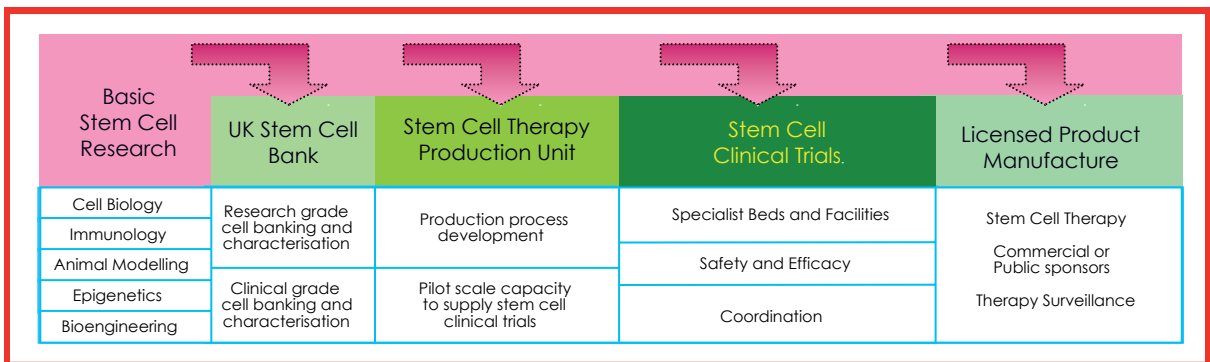
¹Based on costs of administering of a sub-committee of UKCRC for coordination of stem cell research funders.

5.4.2 The UK Stem Cell Cooperative

One of the crucial elements currently missing from UK stem cell research is a national cooperative, network or forum, for the interaction of scientists, clinicians, ethicists, policy-makers, regulators and commercial organisations with an interest in stem cell research. Stem cell researchers have recognised the need for such associations and established them at regional levels, such as the Scottish Stem Cell Network, the East of England Stem Cell Network and the London Regenerative Medicine Network. A UK-wide cooperative would promote the exchange of ideas and actively facilitate collaboration within both the public and private sectors across the breadth of UK stem cell research.

The UK Stem Cell Cooperative should host regular meetings and establish efficient mechanisms to exchange information and ideas in the area. The Cooperative should also work with the International Stem Cell Forum on the characterisation of stem cell lines, the ethical landscape and intellectual property issues.

Recommendation 10: The Government should allocate additional funding to establish *The UK Stem Cell Cooperative*, to maximise the cross-fertilisation between those involved in the sub-disciplines of UK stem cell research.



Projected Cost Range of UKSCI Recommendation 10: £4.6 – 6M

LOW TRAJECTORY (£M):

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
UK Stem Cell Cooperative ¹	0.4	0.4	0.4	0.4	0.5	0.5	0.5	0.5	0.5	0.5
Cost per year	0.4	0.4	0.4	0.4	0.5	0.5	0.5	0.5	0.5	0.5

HIGH TRAJECTORY (£M):

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
UK Stem Cell Cooperative ²	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Cost per year	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6

¹Based on expenditure for annual national scientific conference, regular regional meetings, internet site, administrative costs.

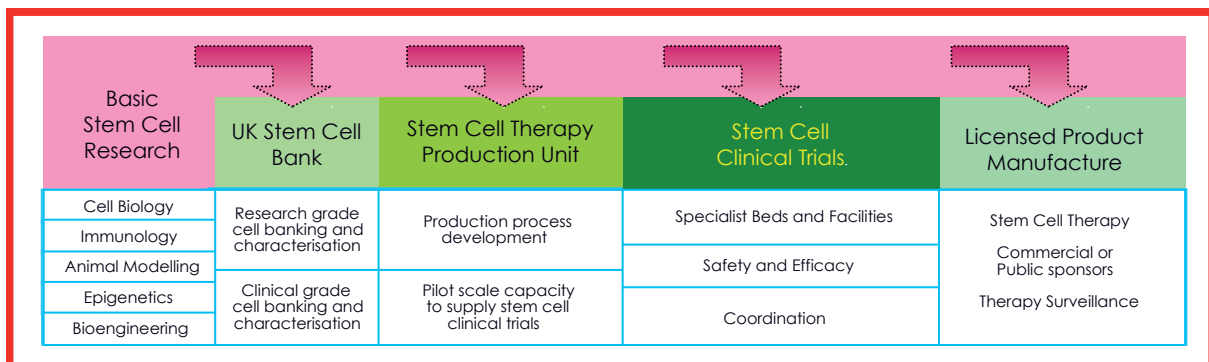
²Based on expenditure for annual international scientific conference, regular regional meetings, internet site, administrative costs.

5.4.3 Public Dialogue

The majority of the UK public are currently supportive of stem cell research, as judged in recent opinion polls and via parliamentary debate. However, as research moves towards the clinic it will be important to ensure that the public is kept aware of developments in a balanced and fair manner. As with all clinical research, the safety of treatments is unknown until clinical research takes place. Any adverse events in stem cell clinical research could unravel public support for this technology.

In accordance with the Council for Science & Technology's 2005 report entitled "Policy through dialogue" , it will be critical for the regulation of stem cell research to take due account of public changes in attitude towards this area. Of key importance in the dialogue with the UK public are (i) the ethical issues surrounding the derivation and laboratory use of embryonic stem cell lines (ii) the use of animal experimentation in stem cell research and (iii) the benefits and risks of stem cell therapies.

Recommendation 11: The Research Councils, charitable funding bodies, and Government Departments should develop a sustained and coordinated programme of public dialogue on stem cell research over the next decade.



Projected Cost of UKSCI Recommendation 11: £5M

COST (£M):

Year	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Annual Public Meeting ¹	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Educational Programmes ²	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
Cost per year	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5

¹Based on expenditure for one annual meeting on stem cell research for a lay audience.

²Based on the development of literature and regional workshops on stem cell research for a lay audience.

5.5 SUMMARISED COSTINGS

In this report, we have made 11 recommendations to act as a strategic guide for public and charity sector investment in UK stem cell research over the next decade. Whilst these recommendations have been designed as a cohesive and comprehensive package of measures, UKSCI believes that the implementation of each one should, by itself, enhance UK stem cell research and, therefore, merits consideration. In the table below, we have summarised the total costs for our programme of recommendations over the next ten years and have projected these to cost in the range of £41M to £104M per annum. We have calculated that pre-existing public and private sector funding bodies' investment to support ongoing research efforts in this area is likely to account for approximately £30M per annum over the next decade [**See Box 11**]. We propose that the UK should maintain this level of investment in ongoing UK stem cell research activity and make an additional investment, ranging from approximately £11M to £74M per annum over the next decade, specifically to supplement the new endeavours proposed in this report. Clearly these cost estimates will need to be updated periodically during the next decade, not least to determine whether the increase in resources required is following a high or low trajectory.

As well as direct funding from Government, Research Councils and private sector funding bodies, UK investment could be augmented from a number of public and private funding sources and enterprises [e.g. **See Boxes 12 & 16**]. With this level of investment in stem cell research, it is probable that a significant portion of discovery and innovation in the entire field of stem cell research will take place in the UK.

Grand Table for Projected Total Cost Ranges of UKSCI Recommendations

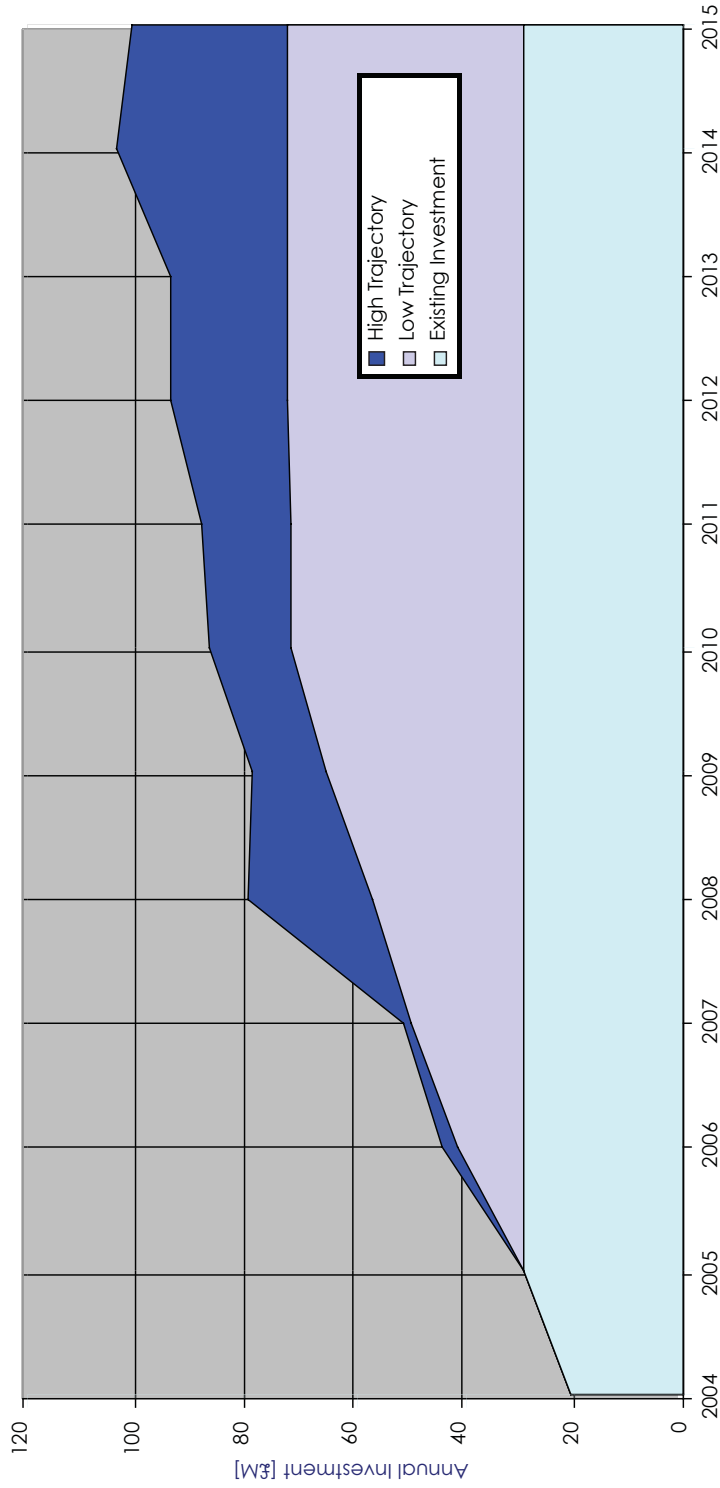
LOW TRAJECTORY (£M):

Recommendation:	Cost over 10 years:	Year									
		2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
1 [Public-Private Consortium]	16.4	0.7	1.3	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8
2 [UK Stem Cell Bank]	17	4.6	1.2	1.2	1.3	1.3	1.4	1.5	1.5	1.5	1.5
3 [Stem Cell Centres of Excellence]	36	4	4	2	2	4	4	4	4	4	4
4 [Cell Therapy Production Units]	12.2	2	1	1	1	1.2	1.2	1.2	1.2	1.2	1.2
5 [Basic Stem Cell Research]	200	20	20	20	20	20	20	20	20	20	20
6 [UK Stem Cell Foundation]	83	2	5	7	9	10	10	10	10	10	10
7 [Full NHS Costs]	265.6	6.4	16	22.4	28.8	32	32	32	32	32	32
8 [Regulatory Measures]	5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
9 [UK CRC]	1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
10 [UK Stem Cell Cooperative]	4.6	0.4	0.4	0.4	0.4	0.5	0.5	0.5	0.5	0.5	0.5
11 [Public Dialogue]	5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Total cost:	645.8	41.2	50	56.9	65.4	71.9	72	72.1	72.1	72.1	72.1

HIGH TRAJECTORY (£M):

Recommendation:	Cost over 10 years:	Year									
		2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
1 [Public-Private Consortium]	31.3	1.0	1.7	2.7	3.7	3.7	3.7	3.7	3.7	3.7	3.7
2 [UK Stem Cell Bank]	20.8	5.9	1.4	1.4	1.6	1.6	1.7	1.8	1.8	1.8	1.8
3 [Stem Cell Centres of Excellence]	70	4	4	6	4	6	8	8	8	12	10
4 [Cell Therapy Production Units]	43.4	3	1	4	2	5.2	3.2	6.4	4.4	8.6	5.6
5 [Basic Stem Cell Research]	272	20	20	22	24	26	28	30	32	34	36
6 [UK Stem Cell Foundation]	87	2	5	10	10	10	10	10	10	10	10
7 [NHS R&D Costs]	278.4	6.4	16	32	32	32	32	32	32	32	32
8 [Regulatory Measures]	5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
9 [UK CRC]	1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
10 [UK Stem Cell Cooperative]	6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
11 [Public Dialogue]	5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Total cost:	819.9	44	50.8	79.8	79	86.2	88.3	93.6	93.6	103.8	100.8


Projected Cost Ranges for UK Stem Cell Research



The graph above plots projected annual investment in UK stem cell research from 2004-2015. 'High Trajectory' and 'Low Trajectory' plots are based on figures from the "Grand Table for Projected Total Cost Ranges of UKSCI Recommendations". Annual investment figures for 2004 & 2005 are based on figures in Box 11. 'Existing Investment' plots investment in UK stem cell research based on the maintenance of 2005 levels of spending between 2006-2015.

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