Government response to the House of Lords Select Committee report on stem cell research / presented to Parliament by the Secretary of State for Health by Command of Her Majesty, July 2002.

DEPARTMENT OF HEALTH

GOVERNMENT RESPONSE TO THE HOUSE OF LORDS SELECT COMMITTEE REPORT ON STEM CELL RESEARCH

Presented to Parliament by the Secretary of State for Health
By command of Her Majesty
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GOVERNMENT RESPONSE TO HOUSE OF LORDS SELECT COMMITTEE REPORT ON STEM CELL RESEARCH

FOREWORD

On 7 March 2001, the House of Lords agreed a motion appointing a Committee "to consider and report on the issues connected with human cloning and stem cell research arising from the Human Fertilisation and Embryology (Research Purposes) Regulations." It published its report on 27 February 2002.

The report is extremely timely as advances in stem cell research are being reported in both the scientific media and popular press at a rate unimaginable even five years ago.

The reason for such interest is the potential that these cells possess. Stem cells are the very early cells that can develop into almost all other types of cell and tissue. They occur in the early (5-day) embryo when it is a tiny ball of about 100 cells before it implants in the uterus. These are embryonic stem cells or "ES cells".

Stem cells also occur in significant numbers in some tissues in the developing fetus and in cord blood at birth. They can also be found in some adult tissue, e.g. bone marrow, but they are difficult to isolate, being present in very small numbers. Conventional wisdom has been that these non-embryonic cells have a restricted potential to develop into new cells and tissues but recent findings have highlighted the importance that they may have too.

Because of their ability to differentiate into different cells and tissues, stem cells hold out exciting prospects for the development of new cellular based treatments. Some stem cells (e.g. bone marrow stem cells) are already used for some treatments of cancers.

The potential of stem cells as a source of new tissue for the repair of diseased or damaged tissues in the future could eventually bring major health benefits. The use of stem cells in this way has already been demonstrated in principle in animal studies. In 2000, the Chief Medical Officer's Expert Group concluded that repairing nerve cells lost in Parkinson's Disease and Alzheimer's Disease, replacing insulin-producing cells in diabetes, changing the outcome of spinal cord injury and multiple sclerosis, replacing lost heart muscle cells in cases of congestive heart failure, bone cells in osteoporosis and liver cells in cases of hepatitis or cirrhosis all seemed realistic prospects if research fulfilled its potential. The hope is that tissues derived from stem cells will be used to develop treatments for diseases and injuries that are currently incurable.

Development of Stem Cell Research

Stem cell research is not a new phenomenon. Early studies in mice in the late 1950s provided the first evidence for the existence of pluripotent embryonic stem cells (those that can develop into almost all other cell types or tissues). The first groups to isolate and successfully culture mouse ES cells were led by Martin Evans at the University of Cambridge and Gail Martin at the University of California in 1981.

Work on haematopoietic stem cells (those that produce the cells of the blood and marrow) developed in parallel from the 1950s onwards, the first bone marrow transplantation taking place in 1969 on a patient with leukaemia. The 1980s saw the first stem cell transplants using cells collected from peripheral blood followed in 1988 by the first transplant using umbilical cord blood.

Stem cells are already an important element in medical care. Bone marrow transplantation depends on the presence of stem cells in the bone marrow, which naturally re-populate the white and red blood cells and blood platelets. This is particularly crucial after cancer chemotherapy. About 75% of all bone marrow stem cell transplants carried out are for patients with some form of cancer.

In 1996 James Thomson of the University of Wisconsin was the first to culture ES cells from non-human primates. His group followed this in 1998 by successfully culturing human ES cells from 5 day stage embryos grown in the laboratory using embryos donated for research by those for whom they had been created for IVF treatment but which were no longer needed for that purpose.

The availability of human ES cells opens up the possibility of research on cells that have the potential to develop into almost every cell and tissue type in the body. ES stem cells can differentiate to form heart cells, liver cells, spinal tissue, brain cells etc. A key area will be to study the mechanisms that control such development in early embryonic cells, to tease out the genetic and biochemical processes that influence this and to apply such understanding in order to modify adult cells, possibly the patient's own cells. In this way the hope is that new compatible cells and tissues could be created for repair of injury and disease.

Exciting though ES cell research is, it is but one strand of stem cell research. Because adult, fetal and cord blood cells have been available to researchers for longer, the bulk of research being published at present is based on these rather than embryonic stem cells. No one can predict exactly where breakthroughs will come. The Select Committee draws attention to the potential of adult stem cell research. The Government agrees and has been using every opportunity to stress that it wishes to see research with all sources of stem cell advanced in the UK. Stem cell research is not a simple matter of adult versus embryonic cells.

Regulation of Embryo and Stem Cell Research

The UK law on embryo research has evolved over nearly 20 years of public and parliamentary debate, beginning with the Committee of Enquiry chaired by Baroness Warnock from 1982 to 1984.

The Human Fertilisation and Embryology Act, 1990 established the Human Fertilisation and Embryology Authority (HFEA) and made it lawful for embryo research to be carried out, under licence from the HFEA. The purposes permitted were research into abnormalities of the early embryo, infertility, congenital disease, miscarriage and contraception. A power was included in the Act to enable these purposes to be extended by Regulations indicating that the possible wider use of embryos for research at a future date was anticipated.

Following recommendations made by the Human Genetics Advisory Commission and the HFEA in 1998 and the Chief Medical Officer's Expert Group in 2000, the Government introduced new Regulations in 2001. After much public and Parliamentary debate, the Human Fertilisation and Embryology (Research Purposes) Regulations 2001 were passed by large majorities in both Houses on free votes. These permit the HFEA to licence research aimed at increasing knowledge about serious diseases, such as Parkinsons and cancer and at increasing knowledge about the development of embryos.

In February 2002, the HFEA granted the first two licences for embryo research under the 2001 Regulations. The protocols approved will create ES cell lines from embryos originally created for IVF treatment but subsequently donated for research. The cell lines will be used to increase knowledge of embryo development and to enable such knowledge to be applied in developing treatment for serious diseases such as Parkinsons, other neural diseases and pancreatic disease. The cell lines will be placed in the planned Medical Research Council (MRC) stem cell bank for use in future studies.

Cloning

Much has been made, particularly in the media, of the use of cell nuclear replacement (CNR) technology, often referred to as "cloning". The Government's approach to CNR is very clear. Any attempt to use such techniques to create a child by so-called "reproductive cloning" is not acceptable and the Government took action in 2001 to make this a criminal offence with the passing of the Human Reproductive Cloning Act 2001.

The use of CNR in research is quite another matter. We believe that CNR may provide researchers with a powerful means of making progress when studying the fundamental processes of cell development. The Government is satisfied that any embryo research that used CNR is covered by the 1990 Act, a position endorsed by the Court of Appeal in January 2002. (The House of Lords is to hear an appeal against this decision. At the time of publication no date has been set for a hearing of the appeal.)

RESPONSE TO THE SELECT COMMITTEE REPORT

The Government welcomes the report "Stem Cell Research" which was published in February 2002. The Select Committee has done an outstanding job in producing such a comprehensive and well argued report in less than a year.

The report provides a detailed overview and assessment of the issues that have emerged from the recent developments in embryo and stem cell research. The Government wishes to see the outcomes of this research developed under appropriate control so that we can realise the promise of new treatments for life threatening diseases and injuries, many of which are currently without cures.

The area of embryo research is already under comprehensive legal controls operated by the HFEA, a Non-Departmental Public Body accountable to the Secretary of State for Health. Some of the Select Committee's recommendations refer to the HFEA. The Government response will deal with these alongside the rest of the Committee's recommendations.

The Government has considered all of the Committee's recommendations carefully. In responding to each of the recommendations in this document, the chapter headings, paragraph numbering and order given in the Select Committee report are used.

STEM CELL RESEARCH

Paragraph 3.22 (i-iv)

i) Stem cells appear to have great therapeutic potential for the treatment of many disorders that are both common and serious and for the repair of damaged tissue.

ii) Until recently most research on stem cells has focused on stem cells from animals and the derivation of ES cell lines from them; cell lines from human ES cells have the potential to provide a basis for a wide range of therapies.

iii) Recent research on adult stem cells, including stem cells from the placenta and umbilical cord, also holds promise of therapies; and research on them should be strongly encouraged by the Government.

iv) To ensure maximum medical benefit it is necessary to keep both routes to therapy open at present since neither alone is likely to meet all therapeutic needs.

v) For the full therapeutic potential of stem cells, both adult and ES, to be realised, fundamental research on ES cells is necessary, particularly to understand the processes of cell differentiation and de-differentiation.

vi) Future developments might make further research on ES cells unnecessary. This is unlikely in the foreseeable future; in the meantime there is a strong scientific and medial case for continued research on human ES cells.

The Government agrees completely with the Select Committee over the exciting prospects that stem cell research may deliver. Stem cell research has been carried out in the UK for three decades and the discoveries that have already been made have shown the promising potential of stem cells.

It is important to realise that research will require long term investment before this potential can be realised. We believe that the UK is ideally placed to be a leading force globally in this field of research.

The Government is already encouraging funding agencies and other research bodies to consider stem cell research as a priority area for funding.

The Government believes strongly that no single source of stem cells should be worked upon exclusively, but wishes to see research move forward on adult, cord blood, fetal and embryonic cell lines. We are pleased that the Select Committee endorses this approach and recognises that we are not dealing with a choice between one source of cells and another.

The application of ES cells to research aimed at understanding cell development and the processes that control cell differentiation will be crucially important. Such research will help us understand early embryo development as well as providing the knowledge needed to move towards new cell-based treatments for serious disease.

The Government is convinced, as was the Select Committee, that embryonic stem cell research will be an essential component of stem cell research for the foreseeable future.

STATUS OF THE EARLY EMBRYO

Paragraph 4.21

Whilst respecting the deeply held views of those who regard any research involving the destruction of a human embryo as wrong and having weighed the ethical arguments carefully, the Committee is not persuaded, especially in the context of the current law and social attitudes, that all research on early human embryos should be prohibited.

Paragraph 4.22

Fourteen days should remain the limit for research on early embryos.

The Government welcomes the endorsement of the Committee for continued embryo research based on the limits set down in the 1990 Act and the 2001 Regulations. The UK has more than a decade of experience with the most comprehensive set of controls over embryo research anywhere in the world.

The 1990 Act states that a licence under Schedule 2 of the Act cannot authorise the keeping or using of an embryo after the appearance of the primitive streak – the first sign of development of a nervous system. The primitive streak is deemed to have formed within 14 days of development. As the Select Committee states, the stage at which ES cells would be extracted is well before this time and the Government agrees that there is no reason to apply any different time limit.

Paragraph 4.28

Embryos should not be created specifically for research purposes unless there is a demonstrable and exceptional need which cannot be met by the use of surplus embryos.

Schedule 2, paragraph 3(1) of the 1990 Act permits the HFEA to authorise research which involves the creation, keeping or use of embryos for the purposes of research. Schedule 2, paragraph 3(6) states that, "no licence ...shall be granted unless the Authority is satisfied that any proposed use of embryos is necessary for the purposes of the research." In addition, paragraph 3(2) restricts the purposes for which the HFEA may authorise research.

As the Select Committee report states, between 1991 and 1998, 118 embryos were created under licence for research purposes. Research that involves the creation of embryos has been aimed at studying the storage of eggs for subsequent use in IVF treatment and for studies of intracytoplasmic sperm injection (ICSI) and of the use of spermatids. In all cases the creation of embryos was necessary for the research.

As part of the process of obtaining a licence from the HFEA, all research projects using human embryos require approval from an independent ethics committee. In reaching their decision on the ethical acceptability of a research project involving the creation of human embryos, such committees would consider whether the research could equally well be carried out on existing surplus embryos.

The legislation and arrangements for ethical approval of research involving the creation of embryos for research have been in place since 1990. We believe that the existing provisions of the 1990 Act are working well and are sufficiently stringent to achieve what the Select Committee is seeking.

Each research proposal is scrutinised by the HFEA on a case by case basis. The Government will require the HFEA to continue to do this and expects the Authority to give particular attention to any projects that involve the creation of embryos.

Paragraph 5.4

Basic research is a necessary step to developing treatments and facilitating the potential use of adult stem cells and should be permitted under the Regulations in the same way as more directly applied research to which it is designed to lead, provided that it is subject to strict regulation.

The Government agrees with the Committee that basic research as well as applied research should be allowed under the Regulations. The Government is confident that the research purposes laid down in the 1990 Act and amended by the 2001 Regulations will cover the type of research described by the Committee.

Paragraph 5.13

Although there is a clear distinction between an IVF embryo and an embryo produced by CNR (or any other methods) in their method of production, the Committee does not see any ethical difference in their use for research purposes up to the 14-day limit.

We agree that the same limits on embryo research apply regardless of the method of creating the embryo. This view was supported in the Court of Appeal in January 2002 in respect to a judicial review brought by ProLife Alliance. The Government's view is that all embryos, however created, deserve the same protection and that they are subject to the controls and safeguards of the 1990 Act and 2001 Research Purposes Regulations.

Paragraph 5.14

Even if CNR is not used directly for many stem cell-based therapies, there is still a powerful case for its use, subject to strict regulation by the HFEA, as a research tool to enable other cell-based therapies to be developed. However, as with embryos created by IVF for research, CNR embryos should not be created for research purposes unless there is a demonstrable and exceptional need that cannot be met by the use of surplus embryos.

The Government agrees with the Select Committee that CNR may prove to be a powerful tool in our understanding of how cells work and how they may be controlled to repair disease and injury.

However as at Paragraph 4.28 above, the Government believes that the existing controls over embryo research in the 1990 Act and by ethics committees are sufficiently robust to allow the HFEA to oversee this aspect of embryology.

Paragraph 5.20

If CNR is permitted in certain limited circumstances, oocyte nucleus transfer should also be permitted for research purposes.

The Government agrees with the recommendation of the Select Committee on oocyte transfer studies, which is in line with the earlier findings of the Donaldson Committee report of August 2000, "Stem Cell Research: Medical Progress with Responsibility".

Paragraph 5.21(a)

Given the high risk of abnormalities the scientific objections to human reproductive cloning are currently overwhelming.

Paragraph 5.21(b)

There are further strong ethical objections to cloning in addition to the risk of abnormalities, although not all the arguments deployed against reproductive cloning are equally valid. The most powerful are the unacceptability of experimenting on a human being and the familial and child welfare considerations arising from ambiguity of the cloned child's relationship.

Paragraph 5.21(c)

The Committee unreservedly endorsed the legislative prohibition on reproductive cloning now contained in the Human Reproductive Cloning Act 2001.

The Government has already made clear that it will not tolerate attempts to implant a cloned embryo into a woman in the UK. The 2001 Act makes it a criminal offence to attempt to do so. Anyone who attempts reproductive cloning faces either up to ten years in prison or a fine or both.

The Select Committee's endorsement of the action taken by the Government in 2001 is particularly welcome.

Paragraph 5.24

The HFEA has an excellent record in ensuring that IVF clinics comply with the law, and we are satisfied that its regulatory powers, now reinforced by a specific statutory prohibition, provide sufficient protection against the development of CNR leading to reproductive cloning in the United Kingdom.

The Government agrees that the combination of the 1990 Act and the 2001 Act provide a robust defence that prevent reproductive cloning in the UK.

Paragraph 7.22

The Government should take an active part in any move to negotiate an international ban on human reproductive cloning.

Agreed. The UK Government is already supporting a draft UN convention to outlaw human reproductive cloning. The first meetings to discuss this convention took place in February/March 2002 and the UN will return to this issue in September 2002.

Paragraph 8.4

At an appropriate time, perhaps towards the end of the decade, the Government should undertake a further review of scientific developments, particularly of the progress of adult stem cell research and therapies, and of the development of stem cell banks, with a view to determining whether research on human embryos is still necessary.

The Government accepts this recommendation. We will continue to keep developments in this field under review and will work closely with those such as the Research Councils (BBSRC and MRC) who are funding stem cell research.

Paragraph 8.5

The Government should keep the funding of the HFEA under review and ensure that its resources are commensurate with its increased responsibilities.

Agreed. The Government works closely with the HFEA to ensure that appropriate resources are available for its statutory responsibilities. The Government notes however that the Select Committee says in Paragraph 8.5 that "it is too early to judge the effect of the (2001) Regulations on the HFEA's future workload" (only 2 applications to date). We will keep this under review.

Paragraph 8.6

The HFEA and the Department of Health should consider how a review of the outcomes of research licensed under the Act might be undertaken and updated on a regular basis.

The Government agrees with the principle of this recommendation. We note that the Committee refers to the very small number of research applications. To date (June 2002) only 2 licences have been issued and reports on outcomes of these research projects and those that are licensed in the foreseeable future should be easily handled and reviewed in DH and the HFEA using existing mechanisms. The Government will ensure this is done.

Paragraph 8.8

The Department of Health should examine with the HFEA the possibility of drawing up indicative guidance as to what constitutes serious disease.

This is a matter on which Ministers were questioned during the passage of the 2001 Regulations. In both Houses, Health Ministers made clear that they did not believe that guidance in the form of lists of what constituted serious disease would be either helpful or practical.

The Government remains of the view that as every licence application is to be examined by the HFEA on a case by case basis such a list is unnecessary. To date there is no doubt that the types of disease that are being researched under licence from the HFEA - Parkinson's and other neural diseases and pancreatic disease - are "serious". However we will review this with the HFEA as and when the number of research applications increase.

Paragraph 8.15

When the Government bring forward legislation they should consider making express provision for such basic research as is necessary as a precursor for the development of cell-based therapies.

This point was covered in part in Paragraph 5.4 above. The Government shares the views expressed by the Select Committee in their analysis. We will keep this aspect under review but at present have no reason to believe that legislation will be required for the foreseeable future.

Paragraph 8.21

The separation of clinical and research roles should be standard practice for the donation of eggs and embryos. The prohibition in the United Kingdom of payment to donors for gametes has been an important element in preventing undesirable commercialisation of this aspect of assisted reproduction and should be strictly maintained.

We agree with the principle behind the recommendation. Both the Government and the HFEA agree that individuals' treatment should not be compromised in any way by participation in any project of research. The implications of donations for research are made clear so as to help potential participants in research make informed decisions about whether to donate embryos.

The HFEA has attached conditions to the licences it has granted recently under the 2001 Regulations requiring the centre to ensure that a designated individual, who is not directly involved in the individual's treatment, is available to discuss the research project and the possibility of donation. The centre must also ensure that the clinical and research roles are separated so that those advising on clinical decisions are not involved in the research project.

The Government agrees that the prohibition of payment to donors of gametes (other than a small amount towards expenses) should be maintained.

Paragraph 8.23

The Department of Health should consider either establishing a body similar to the Gene Therapy Advisory Committee with oversight of clinical studies involving stem cells, or extending the membership or remit of GTAC to achieve the same ends. The Committee sees no other special need at present for additional regulation of the use of stem cells in the treatment of patients.

The Government shares the Select Committee's view that no additional regulation is needed in this field. In the event that cell therapy medicinal products are developed from stem cells these will be regulated at the clinical trials or licensing stage by the Medicines Control Agency (MCA) under the current legislation.

The Select Committee makes an interesting suggestion in respect to clinical studies. We are pleased that the report recognises and endorses the important role played by the Gene Therapy Advisory Committee in overseeing gene therapy research. However, the comparison to gene therapy reveals a number of key differences with stem cells.

When GTAC was established in 1993 it was able to develop oversight *de novo*, gene therapy being a new development. In contrast, stem cell transplantation using adult and cord blood derived stem cells is a well-established medical procedure. As detailed in the introduction, the first stem cell transplants using cells collected from peripheral blood took place some twenty years ago, followed in 1988 by the first transplant using umbilical cord blood.

Stem cells are already an important element in medical care. Bone marrow transplantation depends on the presence of stem cells in the bone marrow, which naturally re-populate the white and red blood cells and blood platelets. This is particularly crucial after cancer chemotherapy. About 75% of all bone marrow stem cell transplants carried out are for patients with some form of cancer.

The Clinical Trials Directive, agreed in 2001, is to be implemented by 2004 and will cover all clinical trials and the MCA will enforce regulations in this area.

Unlike adult stem cell transplantation, the clinical use of cells derived from ES cells would be a new development. The Government will consider whether any further oversight of such clinical trials involving embryonic stem cells is desirable and will discuss this further with interested parties including regulatory agencies such as the MCA and Medical Devices Agency, industry, the Human Genetics Commission and other interested groups.

Paragraph 8.29

The Department of Health's proposal to establish a stem cell bank overseen by a steering committee, responsible for the custody of stem cell lines, ensuring their purity and provenance and monitoring their use, are endorsed. As a condition of granting a research licence, the HFEA should require that any ES cell line generated in the United Kingdom in the course of that research is deposited in the bank. Before granting any new licence to establish human ES cell lines, the HFEA should satisfy itself that there are no existing cell lines in the bank suitable for the proposed research.

The original recommendation to establish a stem cell bank came from the Donaldson Committee in 2000. Since then the MRC, working with DH and the regulatory bodies, has been making progress in establishing the national stem cell bank and a supervisory body. The Government agrees that if the research community can access accredited cell lines from the bank it will act as an additional protection.

The Research Councils have indicated their intention to make the banking of cells a requirement in any grant award for stem cell research. In respect to ES cells derived from embryos in the UK, The Department of Health has asked the HFEA to consider the use of conditions, as recommended by the Select Committee, in their research licences.

The 1990 Act requires the HFEA to satisfy itself that the use or creation of embryos is necessary before a research licence is given. If suitable ES cell lines are already banked and available for a project, then the HFEA will wish to take this into account before deciding on whether a licence should be granted.

Paragraph 8.33

The HFEA should ensure that the implications arising from the "immortality" of stem cell lines are fully covered in obtaining informed consent from donors giving embryos for the potential establishment of ES cells for research. To prevent future restrictions in using ES cell lines (and therefore minimise the need to generate new ES cell lines) the HFEA should not permit ES cell lines to be generated from donated embryos unless informed consent places no constraint on their future use. Where parents wish to restrict the type of research which can be undertaken, for example specifically for reproductive purposes, the embryos donated should be used for purposes other than the generation of ES cell lines.

The Government agrees that it would be both undesirable and unworkable for conditional consents to be applied to the derivation of ES stem cell lines. These cell lines can survive indefinitely and conditions on the donations could, as the Select Committee suggests, open up all sorts of unwelcome possibilities. The Government agrees that if potential donors wish to place constraints on how ES cells derived from their donated embryo are used, then it would not be appropriate to accept their embryos for such research and the HFEA should not allow this.

It is essential that donors giving embryos for stem cell research should be given thorough and appropriate information. They need to understand that any stem cell lines created may continue indefinitely and be used in many different research projects.

The Government agrees with the Committee that the HFEA should ensure that all of the implications have been fully explored with potential donors.

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