ETHICAL, LEGAL AND SOCIAL ISSUES IN HUMAN STEM CELL RESEARCH, REPRODUCTIVE AND THERAPEUTIC CLONING

A REPORT FROM THE
BIOETHICS ADVISORY COMMITTEE
SINGAPORE

June 2002

FOREWORD

The Bioethics Advisory Committee (BAC) was appointed by Cabinet in December 2000 to examine ethical, legal and social issues arising from research on human biology and behaviour and its applications, and to develop and recommend policies to the Ministerial Committee for Life Sciences on these issues, with the aim to protect the rights and welfare of individuals, while allowing the development of the biomedical sciences for the benefit of mankind.

Since February 2001, the Human Stem Cell Research (HSR) Subcommittee of the BAC has extensively addressed the ethical, legal and social issues arising specifically from human stem cell research, including the issues of human therapeutic cloning and human reproductive cloning.

A thorough public consultation process was conducted to obtain input and views from our Singapore community on these issues. The BAC received written submissions from religious, patient, professional, research and medical groups, held dialogue sessions with the various groups to discuss and understand views, and obtained many letters from the general public. After extensive research, careful consideration of community feedback and much deliberation, the BAC has come up with its recommendations in its report, *Ethical, Legal, and Social Issues in Human Stem Cell Research, Reproductive Cloning and Therapeutic Cloning*.

I would like to extend the Committee's sincere thanks to the expert writers who submitted papers to the BAC, as well as to the numerous community groups and individuals who provided their thoughtful feedback. I would also like to thank my fellow Committee members, especially Chairman of HSR Subcommittee Senior District Judge Richard Magnus, for their commitment and efforts to ensure that the report and its recommendations were responsible and respectful of the wide variety of thoughtful views presented to the Committee.

It is my pleasure to present to you the BAC report on human stem cell research and cloning in Singapore.

Prof Lim Pin
Chairman
Bioethics Advisory Committee
June 2002

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EXECUTIVE SUMMARY

INTRODUCTION

1 In December 2000, the Bioethics Advisory Committee ('BAC') was appointed by Cabinet to examine the ethical, legal and social issues arising from biomedical research and development in Singapore, and to recommend policies to the Ministerial Committee for Life Sciences on those issues.

2 In particular, the Human Stem Cell Research ('HSR') Sub-Committee was formed under the BAC in February 2001 to specifically deal with the ethical, legal and social issues arising from human stem cell research, and to consider the related issues of reproductive and therapeutic cloning.

3 Since then, the BAC has examined and deliberated on the relevant scientific, ethical, legal and social issues in this area, and undergone an extensive consultation process, culminating in this Report. In addressing these issues, the BAC's fundamental approach is to balance the two ethical commitments: to protect human life and the rights and welfare of the individual, and to advance human life by curing disease.

SCIENTIFIC ISSUES

4 Chapter 2 of the Report deals with the science surrounding human stem cell research and identifies three widely recognised categories of stem cells, namely, embryonic stem cells ('ES cells'), embryonic germ cells ('EG cells') and adult stem cells ('AS cells').

5 ES cells originate from early human embryos and may be obtained from human embryos created by *in vitro* fertilisation ('IVF'), by cloning technique, or from existing ES cell lines. EG cells originate from primordial reproductive cells of developing foetuses, and can be derived from cadaveric foetal tissues. AS cells are derived from certain adult tissues such as the bone

marrow, brain, skin, intestine and blood cells of the umbilical cord at time of birth.

6 The three types of stem cells appear to differ in their ability to specialise into other cell types. At present, ES cells appear to have the greatest potential to develop into nearly any cell type, followed by EG cells and to a much lesser extent, AS cells.

7 The BAC acknowledges the promise of tremendous benefits to mankind held by ES cells, in particular, for research in areas of treatment and therapy, and in the study of human developmental biology.

8 Chapter 3 of the Report discusses the science of cloning, and how cloning technology is linked with human stem cell research. A distinction between reproductive cloning and therapeutic cloning is drawn. Reproductive cloning refers to the application of cloning technology to animal or human cells that result in the creation of a complete animal or human being. Therapeutic cloning describes the use of cloning technology on such cells for therapeutic or research purposes that do not result in the creation of a complete animal or human being. The Report also discusses the potential which therapeutic cloning holds for furthering the understanding and treatment of human diseases.

ETHICAL, LEGAL AND SOCIAL ISSUES

9 Chapter 4 of the Report examines the ethical issues, social norms, theological and philosophical perspectives that arise and impact on human stem cell research. It focuses on the ethical issues of whether human stem cell research, reproductive and therapeutic cloning should be allowed, and if so, the extent thereof. It is acknowledged that there are detailed legal and regulatory issues that arise from positions adopted on the ethical issues, but such legal and regulatory issues will not be covered exhaustively in the Report.

10 The Report identifies the crux of the matter as arising from the ethics of deriving ES cells from human embryos for research purposes. This is closely linked to the on-going debate on the beginning of life, status of life and respect for life. The spectrum of views held as regards this issue is also presented in this chapter.

11 Chapter 5 describes the extensive consultation process undertaken in an effort to understand all aspects of this issue, the concerns and sentiments of local interest groups as well as the views of the general public. A consultation paper was released on 9 November 2001 to 39 religious and professional organisations for their views. Written responses were received and dialogue sessions were held. Papers were also commissioned from a panel of seven local experts, and inputs obtained from the BAC constituted International Panel of Experts.

INTERNATIONAL PERSPECTIVES

12 Chapter 6 charts a comprehensive survey of perspectives and positions adopted by countries worldwide on the issues of human stem cell research, reproductive and therapeutic cloning. These views were extracted from various sources, including legislation and guidelines commissioned by ethics committees, as well as news reports. The study revealed that different countries adopted diverse and often conflicting positions, and that ethical positions adopted in one society may not be accepted in another.

DELIBERATIONS, CONCLUSIONS AND RECOMMENDATIONS

13 Chapter 7 of the Report begins by presenting an overview of the areas of concern that arise from human stem cell research, reproductive and therapeutic cloning. It acknowledges that there are serious ethical issues that have to be addressed and understands that social norms, theological perspectives and philosophical persuasions all shape the answers given by each society in response to these difficult questions.

14 As a starting point, two broad ethical guiding principles accepted by most responsible societies in discussing the exploitation of science and technology, namely that the results must be just and sustainable, were adopted by the BAC as a conceptual framework in formulating its recommendations. The BAC views human stem cell research as having much potential benefits to offer to mankind, and that such research is important in the major areas, namely treatment and therapy, and in the study of human developmental biology.

15 Concerning the derivation and use of stem cells from adult tissues, the BAC views the process as analogous to the collection of specimens of biological materials from biopsies, and is ethically well accepted. Thus, there are no reservations as regards the derivation and use of AS cells, provided there is no adverse impact on and subject to the informed consent of the donor.

16 The derivation of EG cells from cadaveric foetal tissue however, encroaches upon the contentious issue of abortion. As abortion is permitted by the Termination of Pregnancies Act (Cap 324), the BAC would not revisit this issue. Hence the BAC is of the view that the derivation and use of EG cells is permissible, subject to informed consent of the donor. The decision to donate the cadaveric foetal tissue must be made independently from the decision to abort.

17 The use of ES cells has by far raised the most ethical debates. Diverse views have been proffered regarding the status of a human embryo, ranging from the absolute view that human life with full personhood begins at conception, to the view that the early embryo is only a clump of cells and research using the embryo is ethical in the light of the potential benefits to mankind.

18 Taking into account the diversity of views, the BAC adopts the intermediate position that a human embryo has a special status as a potential human being, but is not of the same status as a living child or adult. However, such respect is not absolute and may be weighed against the benefits arising from the proposed research.

19 Therefore, the BAC supports ES cell research subject to strict regulation of the means and methods of derivation of ES cells. The BAC takes the view that as a measure of respect and protection for the human embryo, ES cell research should take place only when there is very strong scientific merit in and potential medical benefit from such research. Further, only embryos less than 14 days old should be used for the derivation of ES cells.

20 Currently, existing ES cell lines form a ready source for ES cells without requiring further sacrifice of embryos. In addition, ES cells can be derived from surplus embryos not created for the purpose of research but for fertility treatment, which are no longer required. Rather than allow them to perish, their use in research which would serve a greater good is not lacking in respect for these embryos.

21 ES cells can also be derived from embryos created by IVF or by cloning[1] technology. While there are concerns about creating an embryo solely for research purposes, in the final analysis, the essential task for the BAC is still to weigh the need to respect and protect the human embryo against the potential benefits to be reaped from research. The creation of embryos through therapeutic cloning offers an opportunity to derive stem cells which are immunologically compatible with the person being treated, thereby avoiding the problems of rejection. Therapeutic cloning also enables scientists to learn about the mechanisms of reprogramming adult cells to behave like embryonic stem cells again. In the future, adult cells may be able to be reprogrammed to behave like embryonic stem cells, potentially making it unnecessary to resort to using embryos to derive ES cells. Further, ES cell research today is developing at a fast pace, and the scientific evidence on the need for the use of research embryos is emerging day by day. There is a need to be able to respond effectively to such advances.

[1] The use of the word "embryo" in this case is a further extension of the use of the word which now encompasses post-fertilisation products prior to differentiation of placental from foetal products: later products of development where the early foetal structures are already visible, and this new class of cells derived from cloning technology which are not products of gametic fusion.

22 The BAC is of the view that research can adequately be carried out using the existing ES cell lines, and if necessary, surplus embryos. The creation of human embryos specifically for research can only be justified where there is strong scientific merit in, and potential medical benefit from, such research, no acceptable alternative exists, and on a highly selective, case-by-case basis, with specific approval from the proposed statutory body.

23 As for reproductive cloning, the BAC is of the view that the creation of a human being by any cell nuclear replacement techniques or in any other method should be prohibited as the public policy reasons against this are overwhelming.

24 The BAC recognises that it is crucial to set up a comprehensive legislative and regulatory framework to control human stem cell research, and proposes the setting up of a regulatory body to license, control and monitor human stem cell research in Singapore. The constitution, powers and functions of the legislative and regulatory framework as proposed are set out in Chapter 7. Other features would include provisions for informed consent, protection of donors against inducements, coercion or undue influence, control of commerce and sale of donated materials, and conscientious objection to such research or manner of research.

SUMMARY OF RECOMMENDATIONS

25 The BAC believes that the recommendations would lead to 'just' and 'sustainable' results. The results would be 'just', in that research with tremendous potential therapeutic benefits to mankind will proceed. The results would be 'sustainable' as such research has little biological or genetic impact on future generations, especially with the ban on the reproductive cloning.

Recommendation 1: Research involving the derivation and use of stem cells from adult tissues is permissible, subject to the informed consent of the tissue donor.

Recommendation 2: Research involving the derivation and use of stem cells from cadaveric foetal tissues is permissible, subject to the informed consent of the tissue donor. The decision to donate the cadaveric foetal tissue must be made independently from the decision to abort.

Recommendation 3: Research involving the derivation and use of ES cells is permissible only where there is strong scientific merit in, and potential medical benefit from, such research.

Recommendation 4: Where permitted, ES cells should be drawn from sources in the following order: (1) existing ES cell lines, originating from ES cells derived from embryos less than 14 days old; and (2) surplus human embryos created for fertility treatment less than 14 days old.

Recommendation 5: The creation of human embryos specifically for research can only be justified where (1) there is strong scientific merit in, and potential medical benefit from, such research; (2) no acceptable alternative exists, and (3) on a highly selective, case-by-case basis, with specific approval from the proposed statutory body.

Recommendation 6: For the derivation and use of ES cells, there must be informed consent from the donors of surplus human embryos, gametes or cells.

Recommendation 7: There should be a complete ban on the implantation of a human embryo created by the application of cloning technology into a womb, or any treatment of such a human embryo intended to result in its development into a viable infant.

Recommendation 8: There should be a statutory body to license, control and monitor all human stem cell research conducted in Singapore, together with a comprehensive legislative framework and guidelines.

Recommendation 9: In obtaining consent from donors of cells, gametes, tissues, foetal materials and embryos, the information provided to the donors must be comprehensive, and there must not be any inducements, coercion or undue influence.

Recommendation 10: The legislative and regulatory framework should prohibit the commerce and sale of donated materials, especially surplus embryos. Researchers should not be prohibited from gaining commercially from the products of research, as well as treatments and therapies developed from the donated materials.

Recommendation 11: The legislative framework should provide that no one shall be under a duty to participate in any manner of research on human stem cells, which would be authorised or permitted by the law, to which he has a conscientious objection.

CHAPTER 1

INTRODUCTION

1 Recent developments in human stem cell research have raised hopes of discovering new cures for debilitating and fatal illnesses and to alleviate suffering, holding much promise for the benefit of mankind. At the same time, the developments raise important issues about the ethics of such research.

2 In December 2000, the Bioethics Advisory Committee ('BAC') was appointed by Cabinet to examine the ethical, legal and social issues arising from biomedical research and development in Singapore, and to recommend policies to the Ministerial Committee for Life Sciences on those issues. The BAC's fundamental approach in addressing these issues is to balance two ethical commitments: to protect human life, and to advance human life by curing disease. The constitution of the BAC is attached as **Annex A**.

3 In particular, the BAC was charged with the task of addressing the ethical, legal and social issues arising from human stem cell research, as well as to consider the related issues of reproductive and therapeutic cloning.

4 Under the BAC, the Human Stem Cell Research ('HSR') Sub-Committee was formed in February 2001. The constitution of the HSR Sub-Committee is attached as **Annex B**. A research group was also formed to assist the HSR Sub-Committee in its work. The list of the members of the research group is attached as **Annex C**.

5 Since then, the BAC has thoroughly deliberated on the relevant scientific, ethical, legal and social issues surrounding the use of human stem cell in research, reproductive and therapeutic cloning, culminating in the preparation of this Report.

6 The Report begins with an examination of the science of human stem cell research[1], as well as reproductive and therapeutic cloning[2]. The ethical, legal and social issues were identified[3], an extensive consultation process was undertaken[4] and a detailed study of the perspectives and positions adopted internationally was carried out[5]. The crux of the Report follows with the detailed deliberations of the BAC, and ends with its recommendations[6].

7 In the course of its work, the BAC has received a wide spectrum of views, feedback and comments from the local community, especially those with medical, religious, scientific, ethical and legal interests. In addition, the BAC has received much invaluable input, advice and information from local experts and members of an international panel of experts. The BAC records its appreciation to those who have contributed to its work.

8 Finally, the BAC recognises that its recommendations will have a considerable impact, both locally and internationally. Through adopting a measured approach, the BAC seeks to support Singapore's continued drive to excel in biomedical research and development, while remaining a nation responsible to its people, and to mankind.

[1] See Chapter 2: The Science of Stem Cells
[2] See Chapter 3: The Science of Cloning
[3] See Chapter 4: Ethical, Legal and Social Issues
[4] See Chapter 5: The Consultation Process
[5] See Chapter 6: International Perspectives
[6] See Chapter 7: Deliberations, Conclusions and Recommendations

CHAPTER 2

THE SCIENCE OF STEM CELLS

1 Stem cells are unspecialised cells. They are able to renew, proliferate or reproduce themselves. They are also able to specialise and differentiate into other types of cells with specialised functions.

2 The three widely recognised types of human stem cells are embryonic stem cells ('ES cells'), embryonic germ cells ('EG cells') and adult stem cells ('AS cells').

3 ES cells originate from early human embryos. The potential sources of ES cells are:

(a) human embryos created by *in vitro* fertilisation ('IVF') for assisted reproduction or fertility treatments and subsequently not used or needed for treatment which are donated for research. These are commonly referred to as 'surplus' or 'spare' embryos;

(b) ES cell lines which are propagated serially from ES cells derived from human embryos;

(c) human embryos that are created by IVF with gametes donated for the sole purpose of providing research material. These are commonly referred to as 'research embryos'; and

(d) human embryos[1] created for research by the application of cloning technology[2], such as somatic cell nuclear transfer ('SCNT')[3]. These are also commonly referred to as 'research embryos'.

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[1] The use of the word "embryo" in this case is a further extension of the use of the word which now encompasses post-fertilisation products prior to differentiation of placental from foetal products: later products of development where the early foetal structures are already visible, and this new class of cells derived from cloning technology which are not products of gametic fusion.

[2] The process is also commonly known as 'therapeutic cloning'. See also Chapter 3.

[3] In SCNT, the nucleus of an adult human cell is introduced into an enucleated human ovum.

4 EG cells originate from the primordial reproductive cells of the developing foetuses and may be sourced from cadaveric foetuses.

5 AS cells are found in certain adult tissues, including the bone marrow, brain, skin, intestine and from blood cells of the umbilical cord at time of birth.

6 The ability to specialise into other types of cells differ among ES cells, EG cells and AS cells. ES cells appear to be widely pluripotent, retaining the best potential to develop into nearly any cell type, followed in descending order by EG cells and AS cells. Moreover, ES cells appear highly proliferative, both in the embryo as well as in culture, while AS cells appear nearly quiescent and may be more difficult to maintain and expand in culture. These are important biological differences between ES cells, EG cells and AS cells which impact research. ES cells appear to be the most fundamental and extraordinary of the human stem cells, with the highest research potential.

7 Human stem cell research, especially with ES cells, holds the promise for tremendous benefits to mankind in the major areas of treatment and therapy, and in the study of human developmental biology. In treatment and therapy, there is potential for ES cells to be used to generate specialised cells, tissues and organs, and to treat injury or disease including burns, muscular degeneration, cancer, immunodeficiencies, inherited blood diseases, osteoarthritis, spinal cord injury, diabetes, heart failure, liver failure, kidney failure, Alzheimer's disease, Parkinson's disease, multiple sclerosis, and other neurodegenerative diseases.

8 A five day old embryo, more properly called a blastocyst, consists of a mass of cells. Any particular cell is as likely to become part of the placenta, which is discarded at birth, as to become part of the new life. In the first 14 days, the cells of the embryo have not yet differentiated into tissues. The 'primitive streak' appears around the fourteenth day and develops into the nervous system. From the fourteenth day onwards, the embryo develops other tissues and organs and has the potential to develop into a foetus.

9 As stated above, ES cell lines originate from ES cells drawn from early human embryos. In collaboration with researchers from Australia and Israel, Singapore has successfully developed six ES cell lines for research. These originate from ES cells from five-day old frozen embryos, in excess of clinical application, and donated with informed consent of the donors for research. These original ES cells have been serially propagated, to date, at least 200 times. However, there appear to be concerns that cells from ES cell lines alone may not be adequate when it comes to clinical application, in view of problems such as immunological rejection.

10 Research into human stem cells is in its early stage. Nonetheless, its potential is well acknowledged locally and internationally.

CHAPTER 3

THE SCIENCE OF CLONING

1 Cloning is a general term used to describe processes to duplicate biological materials. For instance, researchers often copy genes or pieces of chromosomes to generate enough identical material for further studies.

2 Reproductive cloning refers to the application of cloning technology to animal or human cells that would result in the creation of a complete animal or human being. In the well known creation of the sheep named Dolly by scientists at the Roslin Institute in Scotland, the genetic material from the nucleus of a specialised cell from an adult sheep was transferred to an egg whose nucleus had been removed. Dolly possessed only the genetic material of the donor, and was genetically identical to the donor. The technique used is known as SCNT[1], and has since been applied to clone other animals. There are also other techniques used for reproductive cloning. The public is most familiar with the use of the term 'cloning' in this context.

3 Therapeutic cloning refers to the application of cloning technology on animal or human cells for research and therapeutic purposes that would not result in the creation of a complete animal or human being. With the success of cloning technology in general, therapeutic cloning of human embryos is thrown into prominence, as human embryos thus created appear to be an invaluable source of pluripotent ES cells. Potentially, therapeutic cloning is a means of deriving stem cells which are immunologically compatible with the person being treated.

[1] See Chapter 2, paragraph 3(d).

4 Apart from its potential value for therapy, therapeutic cloning appears important because it enables research that aids in understanding how adult cells might be reprogrammed to behave like embryonic stem cells. This will eventually make it possible to avoid using embryos as a source of stem cells. In addition, therapeutic cloning furthers understanding about human diseases, and appears important in the study of cell-based treatments.

5 Therapeutic cloning appears to be closely linked to human stem cell research. While it is still a frontier area of research, it hints at tremendous benefits to mankind.

CHAPTER 4

ETHICAL, LEGAL AND SOCIAL ISSUES

1 At the outset, the BAC identified the ethical, legal and social issues for consideration. These are listed in **Annex D**.

2 The BAC acknowledged that ethical questions predominate, and are the fundamental matters to be grappled with. On the critical ethical issues, social norms, theological and philosophical perspectives form important considerations. In turn, the stance taken on these ethical concerns would shape the ambit of and create the foundation for the necessary laws and regulations.

3 In this light, the focus of the BAC was on the ethical issues of whether human stem cell research, reproductive and therapeutic cloning should be allowed, and if so, the extent thereof. The BAC recognised that upon reaching a position on the ethical issues, many legal and regulatory issues would arise. However, any detailed legal or regulatory framework is beyond the ambit of this report.

4 At the heart of the ethics of human stem cell research are the ethics of deriving ES cells from human embryos for research, sparking serious debates on the beginning of life, status of life and respect for life. The creation of human embryos by therapeutic cloning to obtain research material is particularly controversial partly because it has been mistakenly perceived as part of cloning of human beings ie. reproductive cloning.

5 Currently, there is no comprehensive legal framework in Singapore governing research on human embryos. However, there are guidelines, namely the 'Guidelines for Private Healthcare Institutions Providing Assisted Reproduction Services' (Regulation 4 of the Private Hospitals and Medical Clinics Regulations (Cap 248 Rg 1). Under these guidelines, the use of human

embryos below 14 days created through IVF techniques but which are not used in assisted reproduction treatments is permissible, provided stringent regulatory stipulations are met.

6 There are diverse views held as regards the status to be accorded to a human embryo. On one end of the scale is the view that a human embryo has the moral status of a person from the moment of conception, and any activity, including research, which destroys the human embryo, is wrong. *A fortiori,* to create a human embryo only to sacrifice it for research purposes is not acceptable. In addition, any advance in therapeutic cloning is also viewed suspiciously as a slippery slope towards human reproductive cloning.

7 A moderate approach accepts that a human embryo deserves respect, with, however, a range of views on the form of such respect, the purposes for which human embryos should be created, and what protection should be accorded to the human embryo at different stages of embryonic development.

8 At the other end of the spectrum, an early embryo is considered to be a mere collection of cells. There is therefore no objection to any form of human embryonic stem cell research, including therapeutic cloning.

9 It is this controversy that the BAC has to resolve to map the path of human stem cell research, and reproductive and therapeutic cloning in Singapore.

CHAPTER 5

THE CONSULTATION PROCESS

1 With the relevant scientific, ethical, social and legal issues in mind, the BAC embarked on an extensive consultation process, to further understand all aspects of the subject matter, and more importantly, to understand the concerns and sentiments of local interest groups and the general public. The consultation process enabled the BAC to obtain very comprehensive information, especially on theological, social and cultural sensitivities, for the purposes of its deliberations. The process is described below.

Consultation with Experts

2 The BAC recognised that advice from experts was necessary in the search for balanced decisions. The BAC identified a panel of seven local experts, which comprised scientists and sociologists, and commissioned them to provide papers on the subject in the local context within their areas of expertise. The scientists were asked to discuss the type and extent of research currently conducted in Singapore, and the technical advances and constraints which they faced. In addition, the scientists and sociologists were asked to provide input on the ethical, legal and social issues that could arise from such research.

3 The list of commissioned papers and the experts consulted are as follows, and the commissioned papers are attached at **Annex E**:

(a) 'Adult Stem Cells'

Dr Hanry Yu, Associate Professor, Department of Physiology, Faculty of Medicine, NUS; Dr Karen Chong Mei Teck, Registrar, Department of Cardiothoracic Surgery, National Heart Centre; A/P James Goh, Research Director, Department of Orthopaedic Surgery, National University of Singapore.

(b) 'Umbilical Cord Stem Cell – Science'

Prof Ng Soon Chye, Department of Obstetrics & Gynaecology, Faculty of Medicine, National University of Singapore.

(c) 'Human Embryonic Stem Cells – Science & Ethics'

Prof Ariff Bongso, Research Professor, Department of Obstetrics & Gynaecology, Faculty of Medicine, National University of Singapore.

(d) 'Ethical Considerations in Stem Cell Research'

A/P John Elliott, Department of Social Work & Psychology, National University
of Singapore.

(e) 'Somatic Cell Nuclear Transfer (Cloning) – Science & Ethics'

Prof Ng Soon Chye, Department of Obstetrics & Gynaecology, Faculty of Medicine.

(f) 'Preimplantation Genetic Diagnosis'

Dr Christine Yap, Obstetrician & Gynaecologist, Department of Obstetrics & Gynaecology, Singapore General Hospital.

(g) 'Legal and Ethical Issues Pertaining to Preimplantation Genetic Diagnosis'

Dr Christine Yap, Obstetrician & Gynaecologist, Department of Obstetrics & Gynaecology, Singapore General Hospital.

4 At the same time, the BAC constituted an International Panel of Experts, comprising Dr Bernard Lo (Director, Program in Medical Ethics, University of

California, San Francisco, USA) and Professor Martin Bobrow (Head, Department of Medical Genetics, University of Cambridge, UK). The BAC was in close consultation with them to obtain objective and constructive feedback.

Consultation with Local Interest Groups

5 The BAC also recognised that engagement of local interest groups was critical. The BAC released a consultation paper on 9 November 2001 to 39 religious and professional organisations for their views. The list of the organisations consulted is attached as **Annex F**.

6 In the consultation paper, the BAC expressed its support for human stem cell research using AS cells and EG cells. On the issue of reproductive cloning of human beings, the BAC was of the firm view that this should not be allowed. The BAC would however, be prepared to support therapeutic cloning, but only if carried out under strictly defined regulations and controls, and only for the purposes of human stem cell research, and not for the purposes of creating a human embryo for reproductive cloning. This same stringent criteria and control were to apply to creating research embryos by IVF. The consultation paper also discussed research using ES cells. The BAC proposed that it would be acceptable to use ES cells obtained from early embryos, not more than 14-days old, in order to carry out serious scientific research which has the potential to benefit mankind.

7 A total of 25 written submissions were received from the religious and professional organisations and are attached as **Annex G.**

8 All 39 organisations were invited to attend dialogue sessions with the BAC. At each session, there was an opportunity for their views and concerns to be discussed and clarified. A list of the organisations and their representatives who attended the dialogue sessions is attached as **Annex H.**

9 Altogether, three dialogue sessions were held on 27 December 2001, 3 January 2002 and 7 January 2002. Three press briefings were also held to

inform the public of the progress of the BAC's consultations with the organisations.

Consultation with the General Public

10 Finally, the BAC recognised that consultation with the general public was also critical. Since August 2001, the BAC has maintained a website containing information about human stem cell research, reproductive and therapeutic cloning. Comments from the public were received through the website. Over 6700 hits were recorded since its inception.

11 On 7 December 2001, the BAC and the Feedback Unit, Ministry of Community Development and Sports, jointly held a focus group discussion session. 39 participants of different races, ages and occupations, were selected by the Feedback Unit to attend, and they provided a range of views for consideration. A report of the discussion was prepared by the Feedback Unit, which is attached as **Annex I**.

12 Finally, members of the public were invited through the mass media to furnish views, and the BAC received letters from members of the public.

CHAPTER 6

INTERNATIONAL PERSPECTIVES

1 The tensions between the potential benefits conferred to mankind and the ethics of human stem cell research, reproductive and therapeutic cloning have also sparked intense debate internationally. In addition to embarking on an extensive local consultation process, the BAC examined in detail the perspectives and positions adopted by countries and organisations worldwide.

2 The BAC obtained information from various sources, including legislation, guidelines, reports and recommendations of ethics committees, and news reports and articles. The study revealed that different countries adopted diverse views and positions, serving to highlight the diversity in our global and pluralistic society. Indeed, ethical positions adopted by one country may be deemed unacceptable in another, and vice versa. To illustrate the spectrum of views, the positions of a major organisation and some large jurisdictions are described in detail below.

UNESCO's report

3 UNESCO's Report by the International Bioethics Committee (IBC)[1] accords recognition to the diverse opinions on the ethical acceptability of human stem cell research and recognises that the solutions adopted by different countries may differ. Ethical debate of human stem cell research should be carried out at appropriate national regulatory levels, reaching, if possible, a consensus on 'the limits of the permissible'. This should be coupled with an on-going process of education and information, and also dialogue within the society with concerned parties.

4 UNESCO recommends that whatever the form of research involving embryos, if allowed, should be carried out within a regulatory framework with

[1] United Nations Educational, Scientific and Cultural Organisation (UNESCO), "The Use of Embryonic Stem Cells in Therapeutic Research", Report of the International Bioethics Committee (IBC) on the Ethical Aspects of Human Embryonic Stem Cell Research, 6 April 2001.

appropriate guidelines and controls, giving due weight to ethical considerations. As the dignity and rights of both parental donors of embryos should be given particular attention, the donation of embryos should only come after the implications of research are fully disclosed and subject to free, informed consent having been obtained. New and alternative technologies for obtaining human stem cell lines (such as from adult stem cells or nuclear transfer techniques) in the area of therapeutic transplantation research should be considered, with a careful weighing of the advantages and risks. In this respect, nuclear transfer should only be used for therapeutic research.

5 UNESCO's Report also states that in all aspects of research involving human embryos, importance must be given to the respect of human dignity and also in respect of the principles set out in the Universal Declaration of Human Rights (1948)[2] and the Universal Declaration on the Human Genome and Human Rights (1997)[3].

United Kingdom

6 In the United Kingdom, the Human Fertilisation and Embryology Act 1990 ('the Act') allows the creation and use of human embryos up to 14 days old for research purposes. Amendments made to the Act (Schedule 2 paragraph 3(2))[4] have widened the scope of research to include therapeutic cloning. All such research is subject to a licence being issued by the Human Fertilisation and Embryology Authority (HFEA), with other strict conditions under the Act. In addition, the conduct of such research is governed by guidelines issued by the Department of Health and a wide range of professional bodies.

7 The Act does not distinguish between embryos created by IVF and those created by SCNT. However licenses will be issued only if the HFEA is satisfied that such research involving the creation of an embryo is necessary for the purposes of the project and that the project is within the list of specified

[2] Article 3 proclaims a right to life in general.
[3] Article 1 proclaims that "Practices which are contrary to human dignity such as reproductive cloning of human beings shall not be permitted".
[4] Human Fertilisation and Embryology (Research Purposes) Regulations 2001.

purposes. To date, the HFEA has not received any application to conduct research involving the creation of an embryo using cell nuclear replacement. Reproductive cloning is not expressly banned by the Act, as the HFEA believes that the current regulation and guidelines offer sufficient protection.

8 The Act does not apply to the keeping of, or research on, human stem cell lines after extraction from embryos. Stem cells derived from adult tissue are governed by the Human Tissue Act 1961. Stem cells derived from foetal tissue (EG cells) are governed by the Code of Practice on the Use of Foetuses and Foetal Material in Research and Treatment (the "Polkinghorne Code of Practice")[5]. All research proposals must be approved by a research ethics committee.

9 The Nuffield Council on Bioethics, in addressing ethical issues in human stem cell therapies, has concluded that the removal and cultivation of embryonic stem cells from donated embryos do not indicate a lack of respect for them. The Council was also of the view that there was no moral distinction between embryo research into reproductive and diagnostic methods, and research into potential therapies. The Council therefore recommends that research involving human embryos be permitted for the purpose of developing tissue therapies from the derived ES cells. As regards the creation of additional embryos, the Council expressed the view that while there was sufficient and appropriate donated embryos from IVF treatments available, there would be no compelling reason to allow such creation to increase the number of embryos for ES cell research or therapy. It was also emphasised that informed consent as regards stem cell research and subsequent use of the developed cell line must be obtained from the donors of foetal material and embryos from which ES cells are derived, as a safeguard to protect these donors who could in theory, be identified by DNA analysis. The Polkinghorne Code of Practice, which this report endorses, requires such consent to be in the written form.

[5] Drawn up by the Polkinghorne Committee in 1989.

The United States of America

10 The position in the United States is unique. Privately funded research projects are not subject to any restriction, whilst research using public funding is regulated. In 1998, the National Bioethics Advisory Commission was charged with the task of conducting a thorough review of the issues associated with human stem cell research. In its Report produced in 1999[6], the Commission recommended that federal funding be allowed for research involving the derivation and use of human EG cells from cadaveric foetal tissue, but not for research involving the derivation or use of human ES cells from embryos created solely for research purposes using IVF or SCNT.

11 The position in the United States, as at 10 August 2001, supports limited public funding for research on human embryonic stem cells obtained from established human stem cells lines only. Following from this, the National Institute of Health (NIH) established a Human Embryonic Cell Registry to list human embryonic stem cells meeting the eligibility criteria, in order to grant funding for such research[7]. Before federal funding is granted, each request for federal funding must cite one of the human embryonic stem cell lines listed on the NIH Registry, meet existing scientific and technical merit criteria and must be recommended by the National Advisory Council. In contrast, privately funded human stem cell research remains free from control. Reproductive cloning is forbidden with federal funding. Although there are no legal barriers to carrying out reproductive cloning with private funds, there is a voluntary moratorium in place.

Japan

12 In October 2001, the Japanese government approved guidelines governing therapeutic cloning, embryonic research and stem cell research. The guidelines require researchers to, *inter alia*, obtain individual consent before

[6] "Ethical Issues in Human Stem Cell Research", USNBAC, Rockville, Maryland 1999.

[7] US National Institute of Health, NIH Guide: "Notice of criteria for federal funding of research on existing human embryonic stem cells and establishment of NIH Human Embryonic stem cell registry", 7 November 2001

using stem cells for research purposes. A law in effect as of 6 June 2001 bans reproductive cloning but allows cloning for certain limited purposes.

Australia

13 The House of Representatives Standing Committee on Legal and Constitutional Affairs was tasked to review the report of the Australian Health Ethics Committee (AHEC) entitled "Scientific, Ethical and Regulatory Considerations Relevant to Cloning of Human Beings" and developed its own recommendations, including recommending a regulatory mechanism within which the research could progress. This was presented to Parliament in September 2001, and is at this point in time, still under consideration. The final decision will be made by the Commonwealth, State and Territory Parliaments and a consistent approach nationally is anticipated to be in place by June 2002.

14 The Committee has recommended enactment of legislation to regulate this area of research for both publicly and privately funded research, as well as the setting up of a licensing body. The Committee reiterated that reproductive cloning research directed towards producing a whole human being must be banned. The use of adult stem cells and embryonic stem cells derived from surplus embryos is permitted. The Committee was however of the view that given the number of surplus embryos available, the specific creation of new embryos for research purposes is unnecessary and should perhaps not be permitted[8]. The Committee also set out parameters within which such research should be carried out, if permitted.

15 The Committee recommends that should the final decision permit such creation, a three-year moratorium could be imposed on the creation of embryos via SCNT, as there is currently no therapeutic purpose to be served. To date, research has not identified any specific opportunities that require the deliberate formation of embryos. The Committee further recommended that

[8] The deliberate creation of embryos for research is not permitted under the Western Australia, South Australia and Victoria legislations, and the NHMRC Ethical Guidelines on Assisted Reproductive Technology.

surplus embryos from IVF treatments could be used for research, subject to approval by an international ethics committee, a national licensing body, and adherence to stringent guidelines. It was an unanimous view that research using AS cells should be encouraged and pursued, as this source of stem cells is wholly accepted, even by those who oppose the use of embryos in research.

Sweden

16 There is currently no legislation in Sweden regulating the research on or handling of human stem cells. The Swedish Research Council recognises the lack of or insufficient regulation in respect to human stem cell research and has presented guidelines on the review of such research[9]. Current research and cultivation of human stem cells from adults, umbilical cord blood and aborted foetuses have been invoked under existing laws and regulations. The derivation of adult stem cells for research is regarded as tissue donation, and the use of cord blood constitutes the utilisation of biological material. Research on the derivation of stem cells from aborted foetuses before week 14 may be done only under special circumstances, subject to the consent of the mother and of the National Board of Health and Welfare. The use of surplus embryos from IVF treatment is permissible only if there are no acceptable alternatives and is deemed necessary to advance research on human stem cells. This is subject to informed consent by the donors and the stem cells must be derived from embryos within the 14-day old limit. While the creation of embryos by IVF solely for research purposes is not allowed, the Council is of the view that the creation of embryos via SCNT may be ethically defensible for therapeutic purposes. However such research is incompatible with the Council of Europe's Convention on Human Rights and Biomedicine[10]. The European Union Commission's Advisory Group on Ethics and the Nordic Council of Minister's Bioethical Committee have proposed a renunciation of research with SCNT, even for the purposes of treatment, as this technique is open to misuse.

[9] Swedish Research Council's Guidelines for Research – Ethical review of human stem cell research, 4 December 2001.

[10] The Convention includes a ban on creating embryos for the specific purpose of research.

Other countries

17 Some countries such as Ireland, Costa Rica and Ecuador expressly prohibit research on human embryos, stating that the right to life of an "unborn child" is equal to that of the mother. In other countries, such as Austria, Canada, Finland, Hungary, Italy, Norway, Peru, Switzerland and Tunisia, the creation of human embryos, other than for the purpose of reproduction, is prohibited.

Conclusion

18 The above are illustrations of the diverse views taken by different countries, with regard to human stem cell research, and which were carefully considered by the BAC in coming to its recommendations.

19 A summary of perspectives and positions adopted by other countries worldwide studied by the BAC is attached as **Annex J**.

CHAPTER 7

DELIBERATIONS, CONCLUSIONS AND RECOMMENDATIONS

Introduction

1 Human stem cell research and the advances in cloning technology have emerged as key scientific developments of the end of the last century, holding out the promise of important new therapies and cures for a wide range of debilitating and presently incurable diseases.

2 At the same time, these rapid and fundamental advances have raised difficult and complex ethical issues which have to be addressed by society in order for the science and the new medical treatments arising from it, to proceed in a sustainable fashion.

3 On these fundamental questions, social norms, theological perspectives and philosophical persuasions shape the answers given by each society. Nonetheless, in any ethical discussion on the exploitation of science and technology, two broad guiding principles would probably be accepted by most responsible societies, that the results must be both just and sustainable. 'Just' refers to the obligation to respect the common good, that there must be fair sharing of the costs and benefits. 'Sustainable' refers to an obligation to respect the needs of generations yet unborn. The principles include the concepts of beneficence and nonmaleficence, that of encouraging the pursuit of social benefits while avoiding or ameliorating potential harm.

4 The BAC adopts these broad principles as a conceptual framework. In addition, in a multi-racial, multi-religious and pluralistic society like Singapore, public policy has to be based on a considered weighing and balancing of the spectrum of views held by various sectors. In turn, public policy would create the necessary foundation for laws and regulations. The BAC recognises that with its recommendations that aim to address the ethical

issues, other legal and regulatory issues would arise. However, any detailed legal or regulatory framework is beyond the ambit of this report.

Derivation and use of stem cells from adult tissues

5 Human biological materials, including cells collected in research projects, biopsy specimens obtained for diagnostic purposes, and organs and tissues removed during surgery, have long been used in research to increase knowledge about human diseases and to develop better means of preventing, diagnosing and treating these diseases. The collection and use of such biological materials is ethically well-accepted provided there is no adverse impact on the donor and adequate consent is obtained.

6 By extension, the BAC has no reservations about the derivation and use of AS cells, subject to informed consent sought from the donor. This view was validated in the consultation process. The local experts, religious and professional organisations, as well as members of the public strongly backed research with AS cells. AS cell research is also widely supported in many jurisdictions, including the UK and the US.

Recommendation 1: Research involving the derivation and use of stem cells from adult tissues is permissible, subject to the informed consent of the tissue donor.

Derivation and use of stem cells from foetal tissues

7 EG cells are derived from cadaveric foetal tissues. The ethical acceptability of deriving EG cells is closely tied to the ethical acceptability of abortion. In the main, the local experts, interest groups and the public are of the view that the derivation and use of EG cells should be permitted.

8 However, the BAC observes that abortion remains a contentious issue for certain sectors of society. The National Council of Churches of Singapore (representing the mainline Protestant denominations, other Christian organisations and member churches), The Catholic Medical Guild, and the Sikh Advisory Board countenance only the use of naturally aborted foetuses.

Implicitly, there were reservations about elective abortions. In this regard, the BAC notes that elective abortion is permitted and governed by the Termination of Pregnancies Act (Cap 324). Criminal sanctions apply to those who fail to comply with the Act, which provides safeguards in relation to the abortion process. It is not within the purview of the BAC to revisit this issue.

9 As with the case of donation of adult tissue for the derivation of AS cells, there must be informed consent from the donor of the foetal tissue. In addition, the decision to donate the cadaveric foetal tissue must be made independently from any decision to abort.

10 Again, the BAC believes its position is well supported by the positions taken by other countries. In the US, federal funding is allowed for research involving the derivation and use of human EG cells from cadaveric foetal tissue. Such research is seen to be analogous to the use of foetal tissue in transplantation. In the UK, the use of aborted foetal tissue is permissible, and the Polkinghorne Code of Practice provides guidance relating to the use of such material in teaching, research and therapy. In fact, in Singapore, the Medical (Therapy, Education and Research) Act (Cap 175) governs the donation of any part of a human body, including organs and tissues, upon death. This Act also applies to the donation of organs and tissues from stillborn infants and foetuses.

Recommendation 2: Research involving the derivation and use of stem cells from cadaveric foetal tissues is permissible, subject to the informed consent of the tissue donor. The decision to donate the cadaveric foetal tissue must be made independently from any decision to abort.

Derivation and use of stem cells from human embryos

11 Although promising research is currently being conducted with AS cells and EG cells, this does not replace the need for research using ES cells. ES cells have different properties from EG and AS cells. They are pluripotent, and currently appear to offer the greatest potential in their ability to give rise to almost any cell type. Scientists are largely in agreement that out of the three

types of human stem cells, research with ES cells has the best potential to deliver benefits to mankind. The use of ES cells derived from human embryos has heightened the tension between the commitments to cure diseases and to protect human life.

12 From the local feedback, there were different responses regarding the derivation of ES cells from human embryos, arising largely from divided views on the status of the human embryo. There were strong contentions that a *human* life begins at the moment of conception. This view was held by the National Council of Churches of Singapore, The Catholic Medical Guild of Singapore, the Sikh Advisory Committee and the Singapore Hospice Association. Others held the view that a human life did not begin until some time after conception (eg. four months, according to the Majlis Ugama Islam Singapura).

13 On one end of the scale, the use of any human embryo for research purposes is seen to be unethical and unacceptable on the grounds that an embryo should be accorded full human status from the moment of its conception. Equally, there are views that it would be ethically irresponsible to deny the progress of scientific research that would benefit mankind. For instance, the Buddhist Federation would support such research.

14 The BAC notes that disagreements about the status of the human embryo are not confined locally. Internationally, theologians and scholars, even those within the same faith, differ on the issue[1].

[1] See the National Bioethics Advisory Commission's report 'Ethical Issues in Human Stem Cell Research', at Appendix E – Summary of Presentations on Religious Perspectives Relating to Research Involving Human Stem Cells, page 100, where it was pointed out that although the restrictive 'official' position within the Roman Catholicism opposes EG and ES cell research, individual Catholics have differed in how to interpret the basic convictions in practice. In contrast to the restrictive view for instance, another Catholic might, with the aid of science, look to the reality of the early human embryo, and see that which is not yet an 'individualised human entity with the settled potential to become a human person'. Hence it is sometimes permissible to use it in research, though as human life it must always be accorded some respect. See also Chapter 4, page 50 and Appendix E pages 100-103, where the NBAC stated that other scholars from Protestant, Jewish and Islamic traditions noted that major strands of those traditions support a view of foetal development that does not assign full moral status to the early embryo.

15 The debate about the moral status of embryos has revolved around the question of whether the embryo should be treated as a person, or viewed as a potential life. From a strictly biological point of view, there is not a clear-cut point at which human life begins. Sperm and eggs are living things, and they fuse to form an embryo, which potentially grows into a living person.

16 There is continuous development from independent gametes all the way through to an independent human being. Attempting to define a point at which this new human being *begins* based on embryology is, the BAC concedes, arbitrary.

17 Taking into account the diversity of views on when *human* life begins, the BAC adopts the intermediate position that a human embryo has a special status as a potential human being, but is not of the same status as a living child or adult. Such respect is however, not absolute and may be weighed against the recognised benefits arising from the proposed research.

18 Therefore, the BAC supports ES cell research. However, ES cell research should take place only when there is very strong scientific merit in, and potential medical benefit from, such research. The BAC's other recommendations on the use of ES cells for research are as stated below.

ES cell lines

19 ES cells can be derived from three sources, namely, the existing ES cell lines, surplus embryos and embryos created specifically for research. Existing ES cell lines form a ready source of ES cells, without requiring any further sacrifice of embryos. The BAC recommends that should ES cells be required for research, they should, wherever possible, be drawn first from the existing ES cell lines. In the US, federal funding of research with ES cells derived from approved existing ES cell lines is allowed.

Surplus embryos

20 The BAC, however, also recognises the limitations that may be faced in research using only existing ES cell lines. For example, there are concerns

expressed by the scientific community regarding possible immunological rejections at the stage of clinical application, in view of the limited number of existing ES cell lines. Even at this stage, the scientific evidence points to the necessity for an alternative source of ES cells.

21 Surplus embryos are not created for the sole purpose of research, but for fertility treatment. Where such embryos are no longer required, the options are to let the embryos perish or to use them. In this scenario, to use them in research to pursue wider therapeutic benefits would be an act of greater respect for these embryos. As such, the BAC considers surplus embryos, which would be otherwise discarded, to be a suitable alternative source of ES cells.

22 The BAC's stance is supported by the positions in other jurisdictions. In the UK, the derivation of ES cells from surplus embryos is permitted. In particular, the Nuffield Council on Bioethics expressed the view that the removal and cultivation of cells from surplus embryos is analogous to tissue donation and concluded that such removal and cultivation of cells do not indicate a lack of respect for the embryos. Although federal funding of such research is not allowed in the US, the NBAC supported the federal funding of such research, and put forth this statement[2]:

> 'Research that involves the destruction of embryos remaining after infertility treatment is permissible when there is good reason to believe that this destruction is necessary to develop cures for life-threatening or severely debilitating diseases and when appropriate protections and oversight are in place to prevent abuse.'

23 The BAC endorses such views. The BAC notes that in Singapore today, surplus embryos less than 14 days old can be used for research purposes provided they meet the stringent regulatory stipulations set out under the Guidelines for Private Healthcare Institutions Providing Assisted

[2] 'Ethical Issues in Human Stem Cell Research', at Chapter 4, page 52

Reproduction Services: Regulation 4 of the Private Hospitals and Medical Clinics Regulations (Cap 248, Rg 1). The BAC also observes that there is a fair amount of public acceptance of such research.

Creation of embryos

24 Next, research embryos may be created by IVF, SCNT or other cloning technology. For some, conducting research on embryos that were originally created for reproduction but which were subsequently not needed is easier to justify than is research conducted on embryos that were created for that very purpose. For others, it is difficult to distinguish between what one can do with an embryo created solely for research purposes, and what one can do with an embryo remaining from infertility treatments.

25 The BAC acknowledges that there is a valid distinction to be drawn between surplus embryos and research embryos. The distinction stems from the fact that the latter are created as a means to an end, for use as research material.

26 In the final analysis, concerning the creation of research embryos, the burden on the BAC is the same as in considering ES cell research on the whole - to weigh the need to protect the human embryo against the scientific value of research embryos and the potential benefits to be reaped from research.

27 As for the source of ES cells, there should be a sufficient supply from ES cell lines, followed by surplus embryos. It is unlikely that it would be necessary to create new embryos by IVF for human stem cell research. In the Chief Medical Officer's report in UK, entitled 'Stem Cell Research: Medical Progress with Responsibility', it was recognised that there are examples of research which could not be conducted using surplus embryos, such as to test the viability of sperm or eggs. However, the view was expressed that 'there should be a sufficient supply of spare embryos for such [human embryonic stem cell] research. It may therefore not be necessary to create new embryos by *in vitro* fertilisation for basic research on the extraction of stem cells.'

28 Unlike research embryos created by IVF, there is evidence that research embryos generated by cloning offers an opportunity to derive stem cells which are genetically compatible with the person being treated. Tissues repaired by such ES cells would be more likely to be immunologically compatible with the intended recipient, thereby avoiding the problems of rejection. Therapeutic cloning also enables scientists to learn about the mechanisms of reprogramming adult cells to behave like embryonic stem cells again. In the future, adult cells may be able to be reprogrammed to behave like stem cells, and potentially making it unnecessary to resort to using embryos as a source of stem cells.

29 Nevertheless, ES cell research today is developing at a fast pace, and the scientific evidence on the need for the use of research embryos is emerging day by day. In the UK, the Human Fertilisation and Embryology Act 1990 allows the creation and use of human embryos up to 14 days old for research purposes, subject to a license being issued for such research upon satisfaction of conditions. The regime allows for embryos to be created both by IVF and cloning techniques. Again, in 'Stem Cell Research: Medical Progress with Responsibility', it was stated that as at 1998, 118 embryos have been created for research by IVF. To date, the HFEA has not received any application to conduct research involving the creation of an embryo using cell nuclear replacement. Nonetheless, the regime is flexible enough to respond to advances in science in order to facilitate worthy research to proceed, and yet robust enough to prevent abuse of human embryos.

30 The BAC adopts the position that the creation of embryos for the specific purpose of research should only be permitted after the satisfaction of stringent conditions and guidelines as evaluated by a statutory body to be set up to license, audit and control human stem cell research. In other words, the BAC is of the view that research can adequately be carried out using the existing ES cell lines, and if proved to be required, surplus embryos. As long as there are sufficient and appropriately donated surplus embryos from fertility treatments available for use in research, there are no compelling reasons to allow

additional embryos to be created merely to increase the number of embryos that will be available for ES cell research or therapy.

31 Therefore, the creation of human embryos specifically for research can only be justified where there is strong scientific merit in, and potential medical benefit from, such research, no acceptable alternative exists, and on a highly selective, case-by-case basis, with specific approval from the proposed statutory body.

32 The BAC acknowledges that there is a further debate regarding the permissibility of creating embryos by cloning technology. The fear is that such research may well result in the cloning of a whole human being. The BAC considers that these fears can be allayed by the strict prohibition of any implantation of such an embryo into a womb.

Age of embryo

33 As an embryo develops, the BAC believes the level of respect and protection accorded must increase.

34 In embryology, before five days, the embryo is a mass of undifferentiated cells. Any cell is as likely to develop into the placenta as to be part of the embryo proper. At day 14, the primitive streak appears. This signals the onset of cell differentiation and organ formation, which includes the development of the nervous system[3].

35 Hence, as a further measure of respect and protection for the human embryo, the BAC recommends that only embryos less than 14 days old should be used for the derivation of ES cells. In relation to the existing stem cell lines, only those where the original ES cells that were used to propagate ES cell lines were derived from embryos of less than 14 days old are to be used.

[3] Since the nervous system is not in evidence before day 14, the qualities of pain and sentience in the sense normally understood would not exist before day 14.

36 The BAC notes that the Law Reform Committee of the Singapore Academy of Law has questioned whether pain is an appropriate measure of determining the cut-off period for use of human embryos, as pain is not a determinant in considering whether an offence has been committed against a person. The BAC emphasises that pain is but one factor in relying on the 14-day mark. A more important consideration, as stated above, is that in an embryo's development, before the 14-day mark, the cells of the embryo are as yet undifferentiated into tissues, in that there is no organised development. Taking into account the overall state of development of such an embryo, the BAC considers that the 14-day mark is still an appropriate limit.

Informed consent

37 Having dealt with the extent of the means and methods of deriving ES cells, the BAC moves on to consider the status of donors. There must be informed consent from the donors of surplus embryos, gametes and cells.

Recommendation 3: Research involving the derivation and use of ES cells is permissible only where there is strong scientific merit in, and potential medical benefit from, such research.

Recommendation 4: Where permitted, ES cells should be drawn from sources in the following order: (1) existing ES cell lines, originating from ES cells derived from embryos less than 14 days old; and (2) surplus human embryos created for fertility treatment less than 14 days old.

Recommendation 5: The creation of human embryos specifically for research can only be justified where (1) there is strong scientific merit in, and potential medical benefit from, such research; (2) no acceptable alternative exists, and (3) on a highly selective, case-by-case basis, with specific approval from the proposed statutory body.

Recommendation 6: For the derivation and use of ES cells, there must be informed consent from the donors of surplus human embryos, gametes or cells.

Reproductive cloning

38 Since the birth of Dolly the sheep, the first cloned mammal in the UK in 1996, many sectors of society have expressed great apprehensions and reservations about this technology being used to clone human beings. The argument is that cloning violates respect and dignity of human life and poses safety problems for those born as a result of cloning technology. The UK, US, Germany and many other major countries have banned the reproductive cloning of humans.

39 There is consensus from all sectors in opposing reproductive cloning. The BAC is of the view that the implantation of a human embryo created by any cloning technology into a womb, known as reproductive cloning, or any other treatment of a human embryo intended to result in its development into a viable infant, should be prohibited. There are strong public policy reasons for this position. These include: (a) the view that human reproductive cloning goes against the moral idea that holds that a human being is not to be treated as a means to an end, but only as an end. This translates into the fear that a whole human being may be brought into existence for a utilitarian purpose; (b) that the social and legal implications of reproductive cloning are very serious, including issues of identity and responsibility; and (c) the fear that it will result in a reduction in biodiversity.

Recommendation 7: There should be a complete ban on the implantation of a human embryo created by the application of cloning technology into a womb, or any treatment of a human embryo intended to result in its development into a viable infant.

Comprehensive legislative framework and regulatory body

40 It is critical that human stem cell research be licensed, and subsequently monitored and assessed by an appropriate body, to establish whether the research is delivering the envisaged benefits, as well as to highlight any currently unforeseen concerns and issues which may arise. The professional organisations generally indicated the need for a well-established and effective framework for the control of such research in Singapore. The Singapore Medical Council stated the need to establish a system which may involve the

setting up of a body at a national level as an oversight committee, backed by legislation that provides stiff penalties for any breaches in the guidelines governing such research. This is to ensure that the researchers strictly adhere to the guidelines for stem cell research. The Biomedical Engineering Society (Singapore) proposed that a Register of Researchers in human stem cell research be set up to regulate the practice of research. The Singapore Society for Biochemistry and Molecular Biology noted that the scientific community in Singapore is small, and hence care should be taken to ensure that no conflict of interests arise from composition of the oversight body tasked to monitor the adherence to guidelines on human stem cell research.

41 Given the ethical issues involved in human stem cell research, the public must be assured that such research can be effectively and efficiently licensed, monitored and regulated, with sufficient attention given to the relevant ethical considerations. Strict oversight of human stem cell research is necessary to prevent abuse. This duty is incumbent on Singapore as a responsible nation in an international community. In the UK, research with human embryos is subject to a licence being issued by the Human Fertilisation and Embryology Authority. The BAC recommends that the UK model be used as a basic model, subject to such modifications as necessary for Singapore, as well as refinements found in regulatory systems in other countries.

42 The BAC recommends a regime as follows:

(a) a statutory body be mandated or established with the functions to license, audit and monitor all human stem cell research in Singapore;
(b) the management of the statutory body shall be vested in a board. The Chairman of the Board should not be a person who has been directly involved in stem cell research. The members of the board should be multidisciplinary, including members of the public;
(c) the permissible areas of human stem cell research for which licences may be granted should be research that increases knowledge about the development of the embryo, serious diseases, or enables any such knowledge to be applied in developing treatments for serious diseases. In

granting licences, the body must review the proposals for research, and its protocols, to ensure that they meet the requirements as stipulated above;

(d) strict conditions should be attached to such licences, including conditions on derivation, storage and use of research materials;

(e) the body should be empowered to conduct regular checks and audits to determine whether the research is delivering the anticipated benefits and also to identify any concerns which may arise;

(f) the body should also be empowered to impose sanctions, including criminal sanctions, on those who fail to comply with the laws or regulations; and

(g) there should be provisions governing informed consent, commerce and sale of research materials and conscientious objections by individuals in such research.

Recommendation 8: There should be a statutory body to license, control and monitor all human stem cell research conducted in Singapore, together with a comprehensive legislative framework and guidelines.

Informed consent

43 The comprehensive legislative and regulatory framework must ensure that in all cases, potential donors for stem cell research must be able to make voluntary and informed choices on whether and how to dispose of biological materials. The informed consent must be obtained from donors of any adult tissues from which AS cells are derived, of foetal materials from which EG cells are obtained, of surplus embryos from which ES cells are derived, and of materials for creating embryos for research.

44 In the course of seeking consent, there should not be any financial, therapeutic or other benefits or inducements for the donors or any specified individual, or any coercion or undue influence for the donation. Although the donor is not to be induced to donate any materials, by any financial, therapeutic or other benefits, this does not preclude the donor from receiving treatments or therapies that may be subsequently developed. The extent of information to be provided to each donor in each specific situation will differ, depending on

the particular circumstances of the donation. A set of regulations or guidelines on obtaining informed consent from donors is necessary.

Recommendation 9: In obtaining consent from donors of cells, gametes, tissues, foetal materials and embryos, the information provided to the donors must be comprehensive, and there must not be any inducements, coercion or undue influence.

Commerce and sale

45 Just as the donors of tissues, cadaveric foetal tissues or surplus embryos are not permitted to receive any financial or other gains from the donation of such materials, similarly, researchers to whom such materials have been donated should not be permitted to trade in such donated materials. Nonetheless, researchers should not be prohibited from gaining commercially from the fruits and products of research, as well as treatments and therapies developed from donated materials.

Recommendation 10: The legislative and regulatory framework should prohibit the commerce and sale of donated materials, especially surplus embryos. Researchers should not be prohibited from gaining commercially from the products of research, as well as treatments and therapies developed from the donated materials.

Conscientious objection

46 With diverse views on the ethics of human stem cell research, it is envisaged that on moral or religious grounds, a segment of the research community and the public may not wish to be involved in such research or in a particular manner of such research. Such objections would be legitimate, given that Singapore is a multi-religious and pluralistic society. It is not the remit of the BAC to challenge or reconcile disagreements held from personal moral or religious convictions. As such, every individual should be allowed to make an informed choice on whether to participate in such research, given his or her beliefs. Hence, the legislative framework should provide for such a situation, in that no one should be under a duty to participate in any such research or

manner of research, which would be authorised or permitted by the law, to which he has a conscientious objection. In the UK, there is provision for this within the Human Fertilisation and Embryology Act 1990.

Recommendation 11: The legislative framework should provide that no one shall be under a duty to participate in any manner of research on human stem cells, which would be authorised or permitted by the law, to which he has a conscientious objection.

Conclusion

47 The BAC believes that the recommendations would lead to 'just' and 'sustainable' results. The results would be 'just', in that research with tremendous potential therapeutic benefits to mankind will proceed. The results would be 'sustainable' as such research has little biological or genetic impact on future generations, especially with the ban on the reproductive cloning.

48 The BAC also believes that the recommendations strike a proper balance between allowing research with tremendous potential therapeutic benefits to mankind to proceed while affording a measure of respect and level of protection to human embryos which takes into consideration the diversity of views on the status of the human embryo.

49 Finally, the BAC reiterates that the recommendations aim to address, in the main, the ethical issues of human stem cell research. The BAC recognises that other legal and regulatory issues would arise. However, any detailed consideration of all the potential legal and regulatory issues would be beyond the ambit of this report.

ANNEXES

ANNEX A

BIOETHICS ADVISORY COMMITTEE

Chairman

Professor Lim Pin
University Professor
National University of Singapore

Members

1. Associate Professor David Chan Kum Wah (until May 2001)
   Department of Philosophy, National University of Singapore

2. Mr Jeffrey Chan Wah Teck
   Head, Civil Division, Attorney-General's Chambers

3. Mr Cheong Yip Seng
   Editor-in-Chief, Singapore Press Holdings

4. Associate Professor John Elliott (as of August 2001)
   Department of Social Work & Psychology, National University of Singapore

5. Associate Professor Terry Kaan
   Faculty of Law, National University of Singapore

6. Professor Louis Lim
   Executive Director, Biomedical Research Council, Agency for Science, Technology and Research *(formerly NSTB)*

7. Ms Lim Soo Hoon
   Permanent Secretary, Ministry of Community Development and Sports

8. Mr Richard Magnus
   Senior District Judge, Subordinate Courts of Singapore

9. Professor Ong Yong Yau
   Chairman, National Medical Ethics Committee

10. Professor Tan Chorh Chuan
    Director, Medical Services, Ministry of Health

11. Mr Zainul Abidin Rasheed
    Mayor, North East Community Development Council

ANNEX B

HUMAN STEM CELL RESEARCH SUB-COMMITTEE

Chairman

Mr Richard Magnus
Senior District Judge
Subordinate Courts

Members

1. Associate Professor David Chan Kum Wah (until May 2001)
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   Permanent Secretary, Ministry of Community Development & Sports

5. Prof Tan Chorh Chuan
   Director, Medical Services, Ministry of Health

6. Mr Zainul Abidin Rasheed
   Mayor, North East Community Development Council

ANNEX C

HUMAN STEM CELL RESEARCH SUB-COMMITTEE
RESEARCH GROUP

Members

1. Ms Hoo Sheau Peng
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2. Ms Karen Lee Hwei Mien
   Senior Officer, Biomedical Sciences, Industry Development Division, Economic Development Board

3. Ms Audrey Lim Yoon Cheng
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5. Ms Abigail Ng
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6. Dr Eugene Shum
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7. Ms Stella Tan Wei Ling
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ANNEX D

ETHICAL, LEGAL AND SOCIAL ISSUES FOR CONSIDERATION

A. Science

1. Definition of stem cell

2. The sources of stem cells for research

- What are the sources of stem cells? eg. from embryos, adult tissues etc.
- What are the properties and potential of stem cells from the different sources?
- Is there a need to prefer one source to the other?

3. The sources for embryos

- What are the sources for embryos? eg. in-vitro fertilisation ('spare' embryos from infertility treatment or specially created for research), therapeutic cloning methods (cell nuclear replacement) etc.
- What are the properties and potentials of embryonic stem cells from the different sources?
- Is there a need to prefer one source to the other?

4. Development of an embryo

- What is the developmental history of an embryo after conception?
- Is there a period post conception which is optimal or appropriate for obtaining stem cells?

5. The reasons for stem cell research

- Why must stem cells be used for research?
- What are the potential benefits?
- How real or speculative are the potential benefits?
- Are there any other alternative forms of research?

6. What is the current state of the science and its technologies?

- What are the current areas of research using stem cells?
- What are the achievements to date?
- When would the potential benefits be reaped?

B. Ethical Issues

1. Do the potential benefits justify stem cell research generally?

2. What source of stem cells should be used, and to what extent?

- In particular, should embryonic stem cells be used?
- Are there no viable or adequate alternative sources? Eg. stem cells from umbilical cord, adult stem cells, embryonic germ cells?
- Status of the embryo as 'life'-
- Definition of life under current legislation eg. in relation to the Penal Code, abortion etc?
- What status should be accorded to an embryo?
- Should the embryo be accorded full human status from conception?
- Should the embryo be accorded full human status at a particular stage of development, and if so, when? eg. day 0, day 14 or day 40 etc.
- Would the potential benefits of research outweigh the concerns of 'violation' of the embryo in order to obtain stem cells, and under what circumstances?

3. Should stem cell research be restricted to certain areas of research with certain levels of benefits, eg. for cancer research as opposed to areas of research which are not life threatening, especially in view of the use of embryonic stem cells?

4. What are the rights of those who donate materials for stem cell research? eg. issues of amount and degree of information to be provided to potential donors, informed and genuine consent, privacy and confidentiality, whether donors are to share in the fruits of successful research either by (a) getting treatment; or (b) payments etc.

5. What are the rights, duties and responsibilities of those who handle stem cells for research? Eg. issues of proper use or code of conduct etc.

6. Sources of embryonic stem cells

- Should stem cells from aborted foetuses be used, and under what circumstances?
- Should 'spare' embryos from infertility treatment be used, and under what circumstances?
- Should embryos be created for research in-vitro, and under what circumstances?
- Should there be therapeutic cloning to produce embryos?
- Is there a need to use therapeutic cloning to produce more embryos?
- Are there objections of producing embryos 'genetically identical' to another human being?

- What are the restrictions on the use of therapeutic cloning? In particular, what is the status of reproductive cloning?
- Should the sale and commercial supply of embryos be permitted, and under what circumstances?

7. What happens once a stem cell line has been established?

- What restrictions, if any, should be placed on the use of such stem cell lines? eg. related issues would include xenografting and xenotransplantation.
- Issues with regard to donors of stem cells as per paragraph 4 above.
- Should the sale and commercial supply of stem cells be permitted, and under what circumstances?

8. Should cross-species experiments be allowed? [Embryonic Stem Cells Sub-Committee to clarify whether it should fall under Human Genetics Sub-Committee's purview]

- eg. issues of trans-species fertilisation, inserting animal DNA into human embryos and vice versa.

9. Controls for trials

- To what extent should trials be conducted on animals and humans?
- Issues of informed consent, privacy and confidentiality.
- Should participants be entitled to some benefits or a share in the fruits of success?
- Questions of compensation to persons injured or placed at increased risk as a result of such trials?

C. Legal and Regulatory Issues, and Public Education

1. Should formal legislation be enacted to govern stem cell research, and its subsequent commercial exploitation, according to a position reached on the ethical considerations, and to what extent eg criminal sanctions and penalties?

2. Should there be a regulatory body formed to license, supervise and monitor the research activities taking place within Singapore, whether government funded, private or otherwise?

3. Established stem cell lines can have considerable commercial value. Issues which would arise would include public and private funding, patenting and commercial issues, claims of donors and users of tissue, and how to manage the demand for forms of stem cell therapy.

4. The amount of public education, awareness and understanding that should be raised and the methods of so doing.

ANNEX E

COMMISSIONED PAPERS

- Adult Stem Cells
  Dr Hanry Yu, Associate Professor, Department of Physiology, Faculty of Medicine, NUS; Dr Karen Chong Mei Teck, Registrar, Department of Cardiothoracic Surgery, National Heart Centre; A/P James Goh, Research Director, Department of Orthopaedic Surgery, National University of Singapore.

- Umbilical Cord Stem Cell – Science
  Prof Ng Soon Chye, Department of Obstetrics & Gynaecology, Faculty of Medicine, National University of Singapore.

- Human Embryonic Stem Cells – Science & Ethics
  Prof Ariff Bongso, Research Professor, Department of Obstetrics & Gynaecology, Faculty of Medicine, National University of Singapore.

- Ethical Considerations in Stem Cell Research
  A/P Prof John Elliott, Department of Social Work & Psychology, National University of Singapore.

- Somatic Cell Nuclear Transfer (Cloning) – Science & Ethics
  Prof Ng Soon Chye, Department of Obstetrics & Gynaecology, Faculty of Medicine, National University of Singapore.

- Preimplantation Genetic Diagnosis
  Dr Christine Yap, Consultant Obstetrician & Gynaecologist, Department of Obstetrics & Gynaecology, Singapore General Hospital.

- Legal and Ethical Issues Pertaining to Preimplantation Genetic Diagnosis, Dr Christine Yap, Consultant Obstetrician & Gynaecologist, Department of Obstetrics & Gynaecology, Singapore General Hospital.

ADULT STEM CELLS

Introduction

1. In response to increasing research in stem cells and clinical prospect for their use in the treatment of diseases, the Singapore National HSR-BAC has been set with the task of setting guidelines for the use of stem cells from various sources.

2. Stem cells are cells that can differentiate into different kind of cells each exhibiting different characteristics such as skin, bone, liver, heart and nerve cells etc. Adult stem cells are those that can be found in adult tissues. Bone marrow has long been regarded as the source of adult stem cells. Recently, stem cells have been found in specific tissue such as in the hippocampus of the brain, and olfactory bulb. It is generally believed that the embryonic stem cells have the most potential to derive into all kinds of cells. Going down the differentiation path from the embryonic stem cells are bone marrow stem cells, tissue-specific stem cells, lineage-specific precursor cells, and then terminally differentiated specific cells. Stem cells have the tendency to be maintained in culture for long period of time, with the capacity for expansion into large cell numbers for therapeutic purposes. However, the control of the differentiation path becomes more difficult the further upstream is the stem cell. Therefore, embryonic stem cells have been the most difficult to produce a pure population of cells for therapeutic applications. On the other hand, precursor cells can be induced to become the desired terminally differentiated cells in one step induction. These cells normally have less capacity for cell expansion. Also, it has been difficult to isolate such precursor cells (e.g. hippocampal neurons from the brain) from the patients. Therefore, it has been appealing to have the stem cells that can be taken from relatively abundant source such as the bone marrow, periosteum, fat tissues and induce them to differentiate into specific types of cells under suitable environment and conditions. Adult stem cells taken from tissue biopsy, fat tissue as the leftover of cosmetic surgery or from cadaver has been explored as the abundant source of adult stem cells as well. Some examples of the adult stem cells are hematopoietic stem cells that produce all types of blood cells, skin epithelium and epithelium of the small intestine, neural stem cells, and mesenchymal stem cells that can differentiate into cells of the musculoskeletal system.

3. The balance between the scientific and clinical promise of stem cell research and ethical controversies, national funding and biomedical development in this area are crucial as Singapore seeks to maintain high ethical and moral standard in its development of Biomedical research. The policies set forth is to avoid the negative consequences that may come with market-controlled research by not only assessing the priority of the research but also ensuring institution and implementation of strict guidelines for stem cells research, its application and commercialization.

Source of Adult Stem Cells

- Live donors or patients:
  i. Bone Marrow-derived Stem Cells:

- Researchers in Philadelphia achieved a billion-fold increase in a few weeks for bone marrow stem cells in culture. With Adult bone marrow stem cells now discovered to be very versatile as many researchers have been able to generate all kinds of tissue, it is also important that researchers have found ways to generate large amounts of adult bone marrow stem cells for research. This creates an abundant supply of cells for research and will be useful in subsequent development of supplies for treatment and other research and therapeutic applications.

David Colter *et al.*; "Rapid expansion of recycling stem cells in cultures of plastic-adherent cells from human bone marrow"; *Proceedings of the National Academy of Sciences*, USA 97, 3213-3218, March 28, 2000.

ii. Periosteum-derived Stem Cells:

Periosteum responds to dynamic fluid pressure by proliferating In vitro, *Journal of Orthopaedic Research, Volume 17, Issue 5, 1999, Pages 668-677* Saris D.B.F.; Sanyal A.; An K.-N.; Fitzsimmons J.S.; O'Driscoll S.W.

Periosteally derived osteoblast-like cells differentiate into chondrocytes in suspension culture in agarose, *Anatomical Record, Volume 259, Issue 2, 1 June 2000, Pages 124-130* Bahrami S.; Stratmann U.; Wiesmann H.-P.; Mokrys K.; Bruckner P.; Szuwart T.

Bone and cartilage formation in diffusion chambers by subcultured cells derived from the periosteum. *Bone 1900;181-8*

iii. Fat tissues-derived Stem Cells:

Tissue engineering of bone and cartilage using rat adipo-derived stem cells, *Tissue Engineering, Volume 6, Issue 6, December 2000, Page 689* Huang, J. I. ; Beanes, S. R. ; Zhu, M. ; Lorenz, H. P. ; Benhaim, P. ; Hedrick, M. H.

Multilineage cells from human adipose tissue: Implications for cell-based therapies, *Tissue Engineering, Volume 7, Issue 2, April 2001, Pages 211-228* Zuk, Patricia A.; Zhu, Min; Mizuno, Hiroshi; Huang, Jerry; Futrell, J. William; Katz, Adam J.; Benhaim, Prosper; Lorenz, H. Peter; Hedrick, Marc H.

Multi-lineage cells from human adipose tissue: Implications for cell-based therapies, *Tissue Engineering, Volume 6, Issue 6, December 2000, Page 655* Zhu, M.; Zuk, P. A.; Mizuno, H.; Huang, J.; Futrell, J. W.; Katz, A. J.; Benhaim, P.; Lorenz, H. P.; Hedrick, M. H.

Multi-lineage cells isolated from liposuctioned adipose tissue undergo osteogenesis in vitro and in vivo, *Tissue Engineering, Volume 6, Issue 6, December 2000, Page 689* Zuk, P. A.; Chaudhari, S.; Katz, A.; Benhaim, P.; Lorenz, H. P.; Hedrick, M. H.

- Cadaveric Tissues: Cadavers are potential source of stem cells. Scientists managed to extract immature progenator cells from cadavers.

Fred Gage's group in UCSD; "Progenator cells from human brain after death"; *Nature*, 411: 42-43

Potential Applications of Adult Stem Cells

- Bone marrow stem cells shown to form **liver** tissue. This can be very useful as liver transplants are scarce. The patient's bone marrow stem cells could potentially be used to form liver tissue that would also be rejected by the patient compared with foreign donor organ liver tissue.

Neil Theise *et al.*; "Liver from Bone Marrow in Humans"; *Hepatology* 32, 11-16, July, 2000.

- Bone marrow stem cells have also been shown to generate **neurons**. This could be useful in generating the brain tissue to replenish dopamine producing cells which are deficient in Parkinson Syndrome patients.

J. Sanchez-Ramos *et al.*; "Adult Bone Marrow Stromal Cells Differentiate into Neural Cells in Vitro"; *Experimental Neurology* 164, 247-256.

- A team at the Albert Einstein College of Medicine in New York took rat stem cells from the cortex and injected them into the brains of both normal adult rats and those damaged by stroke. Stroke patients could potentially recover much better from a stroke with the help of stem cells which would form new mature brain neurons.

- Also, other tissues that have been found to be possibly many other types of tissue. Researchers with Osiris Therapeutics and Johns Hopkins University have shown that adult stem cells from human bone marrow have the capacity to regenerate not only more bone marrow, but also numerous other tissue types as well. In culture, the cells were stimulated to form either **bone, cartilage, or fat cells**. The cells appear to have the potential to form other tissues as well, including **tendon and muscle.**

M.F. Pittenger *et al.*; "Multilineage potential of adult human mesenchymal stem cells"; *Science* 284, 143-147, April 2, 1999.

- Apart from bone marrow, other researchers have been successful in isolating stem cells from periosteum and fat tissues, and have demonstrated the pluripotency of these cells to differentiate into bone, cartilage, ligament, tendon and heart muscle cells.

- Bone marrow stem cells have been shown by Drs. Margaret Goodell and Karen Hirschi at Baylor College of Medicine to stem cells taken from the bone marrow of an adult mouse and transplanted into the bone marrow of another adult mouse had the capability to transform into **blood vessels and cardiac**

muscle. This could potentially help millions of heart attack victims with damaged cardiac muscle and prevent heart failure.

Margaret Goodell and Karen Hirschi ; The Journal of Clinical Investigation. June 1, 2001

Technical controversies

4. There have been controversies that adult stem cells can be a replacement for embryonic stem cells. In general, the adult stem cells seem to be limited in proliferation capabilities and the breadth of applications. The source of the cells is also relatively limited. On the other hand, increasing evidences have documented that adult stem cells can give rise to cells beyond their normal developmental lineages so that they are more plastic than previously believed. Since the adult stem cells can be more readily induced to produce relatively pure populations of terminally differentiated cells for therapeutic applications, these adult stem cells would have more immediate applications and interest from the industrial sectors. Therefore, the guidelines that regulate the research and applications involving these cells are also more urgently needed.

Scientific and Medical Considerations

5. Stem cells are found in the body, some more differentiated and committed than others. When stem cells divide, some progeny develop into specific cell types while others remain as stem cells, for the repair of tissues that have undergone wear and tear. These stem cells are capable of continuously reproducing themselves and serve to renew tissue throughout an individual's life.

6. Although feasible, the following should be prohibited:

   i. ***Hybrid*** cloning - human (or animal) embryos generated asexually by somatic cell transfer or similar cloning techniques where the nucleus of an adult human cell is introduced into an enucleated human or animal ovum (ES cells). This may be considered as either adult-hybrid or embryonic (hybrid) stem cells.

      Although there is much promising research and studies suggesting that it is scientifically and technically limited, there is no legal restriction or ethical guideline for this sort of hybrid cell, consent and risks. Although the source is part adult, its hydrid nature alters the ethics governing its development, use and application.

   ii. ***Reprogrammed Adults Cells***
      The derivation of stem cells from reprogrammed adult cells must also be monitored as our knowledge and understanding of cell and organ develop.

iii. *Mixing of human and animal tissues*
Should not be permitted. Must be in compliance with International Regulations and Acts.

7. The need for an Ethical Oversight and Review Committee at the National and Instituitional level and compliance by the private sector with these recommendations is essential.

Legal and ethical issues

8. Since adult stem cells do not involve Human Embryos, the major issues would involve informed consent and analysis of risks associated with the use of such cells in various applications. (NIH guidelines)

9. Provision should be made for not only hydrid, unforeseen but also case-by-case circumstances in aspects relation to the retrieval to the application and all intermediary stages of stem cell research.

Religious Perspective

10. As a multiracial country, Singapore is posed with numerous traditional and religious beliefs. The retrieval, processing and application of stem cells must comply with the general beliefs of these sectors. This may include the following:
    - Respect for the dead
    - Avoidance of cadaveric tissues and cell retrieved from cadavers

    It is recommended that a study on the reactions of different relevant religions towards these issues be commissioned.

Other issues

- Financial issues such as how the public funding can be used for such research.

- Restricted research such as the definitions and scopes of research activities that certainly cannot be carried out such as intentionally removing biopsy samples from patients without well-informed consent for research purpose only.

- Identifier and ownership issues such as who owns the cells and how to track the source of these cells, which tend to tremendous commercial implications later.

- Guidelines for Informed Consent:
  Guidelines for the use and application of ***biopsy*** or ***Cadaveric tissue*** must be in accordance with stem cells research and international organ-tissue retrieval and donation Act. Guardian and proxies of the deceased must have an accurate account of their role in relation to the deceased. The organs or tissues

must be offered with ***no commercial or financial interest*** on the part of the guardians or proxies. Written and informed consent must be obtained from the donor.

- Safety:
  - Precaution to ensure non-oncogenic nature of cell, tissues or organs transplanted or risk of tumors after transplantation.
  - Disease-free
  - Genetically sound- unpredictable mutations
  - Regulation of Human cellular and tissue-based products
  - Purity of the products

- Oversight of the implementation of the guidelines
  An Oversight and Review Committee is crucial and reports of misconduct should be anonymously submitted to encourage individual responsibility in ensuring the highest possible standard is maintained. Free, voluntary and unanimous reporting of misconduct must be supported. The national biomedical research funding bodies should also monitor and ensure strict adherence to guidelines and standards across the country. The National Bio-ethics Oversight and Review Committee would provide the public with additional assurance that research on stem cells are undertaken appropriately. An analogous division to the Criminal Practice Investigation Beureau, a biomedical body looking into breach and misconduct in stem cell research should be set up. This is important as unforeseen outcomes may arise such as hyrid cells created which may no longer be from either the adult or embryo and is allowed to develop. Hence, the duties of the Committee should include:

  i. A review of research protocols
  ii. Certification that the research proposed is in accordance with approved protocols
  iii. Public Registry of approved protocols
  iv. Database of national and private research sponsors for stem cells research.
  v. Track the history and ultimate use of the stem cell and its products
  vi. Establish requirements and guidelines for funding bodies and private sponsors.
  vii. Report annually to the HSR-BAC on the current state of the science of stem cell research, emerging ethical or social concerns associated with ethical research and the adequacy and appropriateness of the recommendations at the time.

- Development of GCP protocol for safe procurement, transportation of tissues and transplantation.

- Guidelines for laboratory to avoid cross contamination and infection.

- Regulations on the prohibition of cross-species experimentation and clinical applications of such experiments that involve human materials.

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UMBILICAL CORD STEM CELL - SCIENCE

1. Umbilical cord stem cells are stem cells collected from the umbilical cord at birth. Normally, the placenta and its contents are discarded after delivery. It has been found that stem cells can be collected from the umbilical cord before the placenta is discarded.

2. Its current use is to repair the bone marrow after treatments for cancer, as it is thought that umbilical cord stem cells are mainly haematological precursor cells.

3. Until now, stem cells drawn from umbilical cord blood have been reserved mostly for treating children. Because an umbilical cord contains only one-tenth as many stem cells as a marrow donation, it was believed there was too little tissue to reconstitute the immune defenses of an adult.

4. However, new research shows that because the umbilical cord cells proliferate so rapidly, they can indeed be used to treat adults and may even replace bone marrow and other sources of stem cells. Moreover, cord blood transplantation "holds the promise of making it so everyone has a donor."

5. Cord blood stem cells are collected by hospitals before placentas are discarded and so do not involve the controversy over use of stem cells from fetuses.

6. Cord blood cells, stored frozen at public stem cell banks, offer other key advantages. They are immunologically "naive," unlike cells from adults, and are thus far less likely to trigger a common, life-threatening complication called graft-versus-host disease.

7. Moreover, cells from newborns are unlikely to contain viruses, unlike most adults.

8. The current research emphasis is on developing ways to make stem cells from cord blood multiply in the lab so there are more cells to transplant.

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As this submission is to be part of the deliberations of the Bio-Ethics Advisory Committee on Human Stem Cell Research Sub-Committee, it will be relatively concise.
This submission is based on a review paper in preparation by Ng et al (2001).

HUMAN EMBRYONIC STEM CELLS: SCIENCE AND ETHICS

INTRODUCTION

1. Every day thousands of people of all ages are admitted to hospitals because of disease of some vital organ. Some of these diseases do not have permanent cures as yet and because of a dearth of transplantable organs, many of these people eventually die. A dramatic example reported by the American Heart Association is that only 2,300 of the 40,000 Americans who needed a new heart got one (Scientific American, 1999). Even in Singapore there is a long line of patients waiting for heart transplants. Cancer, HIV, diabetes and neuro-degenerative diseases are other life-threatening ailments that add to this list.

2. An exciting new strategy is poised to revolutionize treatment for such diseases. The ultimate cell, the human embryonic stem (ES) cell that can be engineered to produce replacement cells of any type, help to create new tissues and eventually new organs for transplantation has been developed. The ES cell commonly referred to as the 'mother of all cells' promises to open a new era in regenerative medicine with tremendous hope for the cure of a variety of incurable diseases. However this new science has been recently surrounded by ethical sensitivities because the source for derivation of such cells are human embryos and this has impeded the progress of this science. This paper will address the science of ES cell biology, critically evaluate the ethical sensitivities and recommend to the Human Stem Cell Research sub-committee policies, with the hope of protecting the rights and welfare of individuals while allowing this science to develop and realize its full potential for the benefit of mankind.

THE SCIENCE OF ES CELL BIOLOGY

What are stem cells?

3. Stem cells are unspecialized cells in the human body that are capable of renewing themselves and also being able to specialize into other new cell types, each with specialized functions.

Sources of human stem cells

4. Several sources of human stem cells have been recognized today. These have been isolated from the preimplantation embryo, fetus and adult. Embryonic stem cells have been confirmed to be widely pluripotent compared to fetal and adult stem cells. Stem cell sources, acronyms and pluripotentiality are shown in Table 1.

Sources for derivation of ES cells

5. Embryonic stem cells can be derived by a number of methods:

(a) Human embryos created by in vitro in fertilization as a method for treatment of infertility. These embryos are excess of fertility need and are voluntarily donated by subfertile couples who no longer plan to use the embryos and do not wish they be donated to other couples or be disposed.

(b) Human fetal tissue following elective abortion.

(c) Human embryos created by in vitro fertilization with sperm and eggs donated for the sole purpose of providing research material.

(d) Human or hybrid embryos generated asexually by somatic cell nuclear transfer of the adult human cell nucleus into an enucleated human or animal egg (therapeutic cloning).

6. Of the above four types, only types (a) and (b) have been utilized.

Human embryonic development

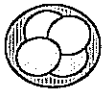
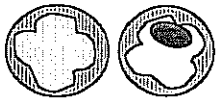
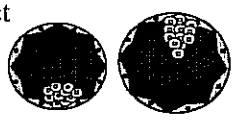
7. Through the technology of in vitro fertilization it has been possible for the first time to observe and accurately describe the stages and timing of early human embryonic development (Bongso et al 1998; Table 2).

Table 1: Sources of human stem cells

Name	Acronym	Source	Pluripotentiality*
Embryonic stem cell	ES	5 day old embryos (Blastocysts)	Widely pluripotent
Embryonic germ cell	EG	First trimester abortuses	Pluripotency not confirmed
Adult stem cell	AS	Adult tissues (Blood, bone-marrow, umbilical cord, liver, brain)	Not widely pluripotent (multipotent)

*Pluripotentiality: ability to specialize into other cell types.

Table 2: Human embryonic stages observed each morning from day 1 to 6

Day (hr)	Embryonic stage	Description	
1 (18-20)	Two Pronuclear stage	Male and female pronuclei present	
2 (48)	Cleavage stage	4 cells	
3 (72)	Cleavage stage Compacting	8 cells discrete 8 cells fusing	
4 (96)	Compacting Compacted Early cavitating	8 cells fusing All cells fused (morula) First signs of blastocoele	
5 (120)	Late cavitating Early blastocyst Expanding blastocyst	Distinct blastocoele, ICM, TE not distinct Distinct ICM, TE Distinct ICM, TE; embryo diameter increased	

ICM: Inner cell mass (future ES cells); TE: Trophectoderm (future placental cells)

8. We now know that optimum numbers of motile sperm have to encounter an egg with its enclosed cell vestments so as to produce optimum fertilization (10,000 sperm per egg per 100 µl of nutrients) (Bongso et al 2000). Interestingly, optimum fertilization is completed in one hour (Gianorrali 2000). Visual evidence of fertilization (the two pronuclear stage) is noticed only at 18-20 hours after sperm-egg interaction. Each pronucleus containing maternal and paternal genetic make-up (23 chromosomes each) have not as yet fused or joined to establish the 46 chromosome state. Fusion of both pronuclei (syngamy) occurs at approximately 20 to 23 hours and the first cleavage division (2-cell stage) occurs at 24-25 hours. This would be the completion of Day 1 of embryonic development. At 48 hours (Day 2) the embryo is a ball of 4 cells, at 72 hours (Day 3) a ball of 8 cells with the cells fusing in some embryos and on Day 4 is the cavitating stage when the first signs of a cavity (blastocoele) is formed. Migration of cells within the embryo takes place between days 4 and 5 to produce on days 5 and 6 blastocysts at various stages of development. The blastocyst is still a ball of cells, but the cells have migrated within the embryo to form two distinct cell layers, the outer cell mass (trophectoderm) and inner cell mass (ICM) (Table 2). The trophectoderm has about 200 cells, which form the future placenta and the ICM about 30 cells that differentiate to form the future foetus. The blastocyst is enclosed in a shell called the zona pellucida. ES cells are isolated at this blastocyst stage from the 30 ICM cells. This 5 day old stage is the best and the most optimal stage for ES cell derivation because the ICM can be visually recognized (Table 2).

How are ES cells isolated and propagated

9. In vitro fertilized frozen surplus preimplantation stage 2 to 5 days old embryos that are not used for clinical treatment are donated voluntarily with informed consent by patients undergoing in vitro fertilization procedures. Frozen instead of fresh embryos are used for ES cell derivation so as to give both husband and wife ample time to think and agree whether such embryos should be donated for this specific research. If the frozen embryos are 2 days old, they are thawed and grown to the 5^{th} day (blastocyst stage) for isolation of the ICM. The ICM is separated by immunosurgery and grown on mouse embryonic fibroblast feeder cell layers. The mouse feeder cells are previously treated with mitomycin-C to

arrest their growth and act only as a supplier of nutrients and specific undifferentiating factors by cell to cell contact. After about 2 weeks, the expanded ICM lump is separated from the feeder layer with enzymes, dissociated into small pieces and re-grown on fresh mouse fibroblast feeder layers. The ICM cells, now called ES cells are continuously grown in this way to expand cell numbers. At alternate generations, an aliquot of ES cells are injected under the testicular or kidney capsule of severely combined immunodeficient (SCID) mice to allow the growth of these cells in 4 weeks into differentiated human cells and tissues including gut (endoderm); cartilage, bone and muscle (mesoderm) and nervous tissue, skin (ectoderm). These three cellular layers (endoderm, mesoderm and ectoderm) have the potential to form all the 210 cell types of the body and the ES cells are then confirmed truly and widely pluripotent. Four such cell lines have already been developed in Singapore with informed patient consent and according to NIH, USA and NUH ethical committee guidelines.

Benefits of ES cells to mankind

10. ES cells hold promise to mankind in three major areas: (1) Transplantation therapy (2) Pharmaceutical development (3) Human developmental biology.

1. Transplantation therapy

The potential therapeutic impact of ES cells in transplantation therapy is enormous because of their capability to produce virtually unlimited quantities of any cell in the body. Additionally, they have the potential to be genetically engineered to prevent their immune rejection by the transplant recipient thereby bypassing the need to provide each recipient with his/her own ES cells via therapeutic cloning. Examples of medically relevant cells that could be developed from ES cells for human transplantation therapy are cardiomyocytes for the treatment of myocardial infarction and congestive heart failure; neuronal cells for the treatment of stroke, Parkinson's and Alzheimer's diseases; blood cells for the treatment of blood related cancers and HIV (after genetically engineering these cells to resist infection by the HIV virus); pancreatic islet cells for the treatment of diabetes; skin cells for the treatment of wounds, burns and for the cosmetic industry; and cartilage cells for the treatment of osteoarthritis.

These clinical applications will involve direct injection of ES cell-derived differentiated cells into the diseased sites. Further research could lead to development of complex multi-cellular solid tissues and organs by encouraging these cells to interact with scaffolds made of degradable polymers.

2. Pharmaceutical development

Permanent stable sources of normal differentiated human cells can be developed for drug screening and testing, drug toxicology as well as new drug target identification and the screening of teratogens (drugs causing birth defects) extending the capability of current screening using animal cell lines, bacterial and laboratory animal systems.

3. Human developmental biology

Since ES cells can be made to differentiate into a variety of functional cell types in a laboratory dish, they offer a unique platform to understand and harness nature's mechanisms of embryonic development, tissue differentiation and repair. Such understanding will contribute to the treatment of fertility disorders, the prevention of premature pregnancy loss and diagnosis and prevention of birth defects. The availability of ES cells may facilitate research in these areas without the need to use human embryos or fetuses.

Unique characteristics of ES cells

i. Wide pluripotency

HES cells can form virtually any cell in the body. They have been shown to form derivatives of all three primary cell layers (ectoderm, mesoderm and endoderm) in immunodeficient SCID mice (Reubinoff et al 2000) and hence have the potential to be directed into gut, cartilage, bone, muscle (heart and other muscle), nerve, skin, pancreas etc. Already differentiated adult stem cells have limited pluripotency to form certain cell types for eg. bone-marrow to heart in the mouse (Orlic et al 2001), bone-marrow to neurons in the mouse (Brazelton et al 2000), bone-marrow to liver in the mouse (Petersen et al 1999).

ii. Self-renewing capacity

Under specific culture conditions ES cells can repopulate themselves while remaining in an undifferentiated state. Their growth in vitro is also prolific and as such once isolated from a few embryos they will be a continuous source of normal pluripotent stem cells. The major benefit of the already developed 4 cells lines from 4 donated embryos is that they not only can be scaled up in large numbers but also can be provided for research worldwide without the need to isolate more cells from embryos or fetal tissue. It has not been possible to maintain long-term self-renewing capacity of adult human stem cells in culture. The ability of ES cells to propagate indefinitely in the undifferentiated state without losing pluripotency is a feature that distinguishes these cells from all other 'multipotent stem cells' discovered todate in the human.

iii. Telomerase expression and immortalization

Telomerase is an RNA-dependent DNA polymerase which when reactivated in normal cells allows their continual proliferation. ES cells express abundant amounts of telomerase. The continuous steady release of telomerase activity in ES cells conveys replicative immortality. Adult stem cells express telomerase at low levels or only periodically and may therefore age and stop dividing with time.

iv. Normal genetic make-up with continuous growth

ES cells maintain a normal genetic make-up even after prolonged growth in vitro. They do not undergo chromosomal changes, as is characteristic of most adult cells grown in vitro. It is not known whether adult stem cells will show such genetic changes with prolonged growth in vitro because as of now no adult stem cell has been serially sub-cultured as a cell-line for many generations.

v. Isolation and availability

ES cells have been isolated from frozen embryos with very high efficiency (eg. 4-cell lines from 7 embryos, ESI). The cells propagated from these existing 4 cell lines are enough for research for all centers worldwide and can be scaled up even further for application because of their prolific growth. (Biocentury, May 2001). Adult stem cells in the human body except for bone-marrow and

umbilical cord cells are very few in number and not easily accessible in the human body. The extent of growth in vitro is yet unknown for all adult stem cells including bone marrow and umbilical cord cells. In some situations like the brain, isolating the stem cells would be difficult and a dangerous procedure itself. For some acute disorders there may not be long enough time to scale up enough cells for treatment.

Current state of ES cell research

11. Undifferentiated human embryonic stem cell lines from embryos have been developed by two groups in the world (Bongso et al 1994; Thomson et al 1998; Reubinoff et al 2000). One group (Thomson et al 1998) has 5 cell lines (with patient consent for research only) with no compliance to NIH ethical guidelines. The other group (Bongso et al 1994; Reubinoff et al 2000) have 2 cell-lines for research (non-NIH compliant) and 4 cell lines for research and application compliant with NIH, MOH, Singapore and NUH ethical committee guidelines. All these cell lines have been serially propagated thus far at least 200 times and have been confirmed pluripotent at all generations by demonstration of human tissues in immunodeficient SCID mice. Whilst it is true that ES cells have the potential to become every cell type in the body, they require certain triggers to persuade them to develop along specific cell lineages. In the embryo for example what cell type a cell will eventually become is determined by a combination of factors including physical forces, electrical charges, hormones and growth factors. All these forces combine to determine the cells future by switching certain genes on and other genes off. Some of these triggers have already been worked out for ES cells and pure nerve and heart cell lines have already been developed that are undergoing characterization in animal models (Reubinoff et al and Mummery et al, unpublished data). These tasks become even more difficult to direct adult stem cells since nothing is presently known as to what factors can de-differentiate already differentiated adult cells.

12. In the mouse, ES cells have been genetically stabilized into heart cells (Klug et al 1996) and modified into nerve cells with retinoic acid (Deacon et al 1998). Recently, beating ventricular-like heart cells from murine ES cells were separated in vitro (Muller et al 2000) and murine ES cells were successfully

directed into insulin-producing cells in vitro (McKay et al 2001). These cells were able to release insulin in the presence of blood sugar. When ES-derived murine nerve cells were transplanted into mice with spinal cord injuries and brain disorders, engraftment of the injected cells into the diseased sites occurred with improvement of nerve function (Deacon et al 1998). Similarly, the transplantation of ES-derived heart cells into the scar tissue of ischaemic adult mouse hearts showed engraftment, improvement of new blood vessel formation (angiogenesis) and improvement of heart function (Klug et al 1996).

13. Getting human ES cells to turn into many cell types targeted against specific diseases is an ongoing area of research. A lack of government funding for this promising area of research has slowed down its progress because of the debate on the ethical issues involved in deriving ES cells from human embryos. Once these issues are cleared, the potential benefits are expected to be reaped at least within the next 10 years.

THE ETHICS OF ES CELL BIOLOGY

Status of the human embryo

14. Just about anything with the label 'embryo' or 'fetus' arouses the concerns of many people about the dignity of human life or human potential. It is important to note that a 5 day old blastocyst is not yet a so called 'embryo'. Any particular cell in a blastocyst is as likely to become part of the placenta, which will be discarded at, birth, as it is to become part of a 'potential person'. Ethics commissions in several countries including the United Kingdom (Warnock report), the USA (NIH Human Embryo Research Panel, 1994), Australia and Denmark have approved research on the human embryo up to 14 days. Up to 14 days it is more correctly called a 'pre-embryo' because the embryo has not differentiated into tissues. At 14 days, a structure called the 'primitive streak' appears which later becomes the brain and spinal cord and which then differentiates embryo from placenta. Before 14 days there is no possibility of pain or sentience and no cells that will definitely become part of an individual.

15. It would not be right to readily dismiss the objections that using embryos for ES cell research is an insult to human dignity. The frozen embryos used for ES cell

derivation are in excess of fertility need and already abandoned by their parents as by-products of other conception attempts. Currently these embryos have a zero chance of ever maturing to human beings. Stem cell research offers the cells more opportunity for life than they would otherwise see (Scientific American, May 2001).

Do the potential benefits justify embryonic stem cell research?

16. Interestingly, knowledge gained thus far from the 4 existing ES cell-lines confirm that ES cells are not only versatile but prolific in their growth. There is virtually no limit to the quantity of stem cells that can be generated from these few cell-lines (BioCentury, May 21, 2001). Interestingly, the efficiency was over 60% to generate these 4 cell lines because they originated from 7 frozen pre-embryos (Bongso and Fong 2001). These cell-lines are now virtually immortal because they have been serially subcultured over 200 times and the available cells can be supplied for researchers around the whole world forever without destroying any additional embryos. Thus future research does not depend upon continued use of pre-embryos.

17. Given the fact therefore that ethical sensitivities are now no more an issue for ES cell research, the potential benefits in the final usage of these cells is tremendous. Because of the versatility of these cells (widely pluripotent) almost any disease has a potential cure by transplantation therapy once target cells or tissues are derived by differentiating these ES cells. ES cell-derived nerve, heart, blood and pancreatic cells will have cures for stroke, Parkinson's disease, Alzheimer's disease, heart diseases, cancers and diabetes. Because ES cells are widely pluripotent, prolific in their growth and 'younger' cells, they would be the gold standard over adult stem cells for replacing bad tissue with good. Even though they are donor cells unlike the patient's own adult stem cells, their histocompatibility genetic make-up can be engineered to prevent rejection after transplantation. However, it is important to note that when attempting to seek clinical benefits as fast as possible the use of both ES and adult stem cells for research should be encouraged because we do not know at this point in time which stem cell will be best suited for a particular disease.

What source of stem cells should be used for research?

18. Both ES and adult stem cells should be used as sources of cells for stem cell research. Even though adult stem cells may be more convenient to use, the scientific fact is that we do not yet know whether the adult stem cells necessarily retain the full plasticity of ES cells. Research should and will continue on adult stem cells and if they ultimately prove as capable as or better than ES cells, it might then be wise to forsake ES cells in deference to the moral debate over whether an embryo is really a human being. Until then, adult stem cell research can only be an adjunct to ES cell work. Polls taken in the USA have suggested that most of the American public think that ES cell research should continue. This means that the American Congress must decide how to balance ethical objections with the potential benefits of ES cell research. Should we ignore research that offers the best hope for treating or curing many illnesses? (Scientific American, May 2001). The overwhelming consensus among the real scientists involved in both ES and adult stem cell research is that no avenue of stem cell research can be safely ignored (The Scientist, May 28, 2001). We simply do not know what types of cells would work best for particular diseases. In January 2001, after contentious debate lasting more than 8 hours the British House of Lords voted overwhelmingly to allow research on ES cells (The Scientist, May 28, 2001).

NIH guidelines for research using human embryonic stem cells

19. On August 25, 2000, the NIH, USA brought into effect its guidelines allowing research on human embryonic stem cells. This was after receiving 50,000 comments from members of Congress, patient advocacy groups, scientific societies, religious organizations and private citizens. (NIH Website, Aug, 2000). In its guidelines the NIH concluded that it was possible that no single source of stem cells is best or even suitable/usable for all therapies. Different types of sources of stem cells may be optimal for the treatment of specific conditions. In order to determine the very best source of many of the specialized cells and tissues of the body for new treatments or cures, it was concluded that it was vitally important to compare the potential of adult stem cells with that of ES cells. Unless all stem cell types were studied the differences between adult stem and ES cells will not be known.

20. The conditions for the derivation and utilization of ES cells from human **embryos** set out by the NIH are described below.

i. The ES cells must be derived from human embryos that were created for the purpose of fertility treatment and were in excess of the clinical need of the individuals seeking such treatment. It must be ensured that the donation of human embryos in excess of the clinical need is voluntary and, no inducements, monetary or otherwise, should have been offered for the donation of human embryos for research purposes. Fertility clinics and/or their affiliated laboratories should have implemented specific written policies and practices to ensure that no such inducements are made available.

ii. There should have been a clear separation between the decision to create embryos for fertility treatment and the decision to donate human embryos in excess of clinical need for research purposes to derive pluripotent stem cells. Decisions related to the creation of embryos for fertility treatment should have been made free from the influence of researchers or investigators proposing to derive or utilize human pluripotent stem cells in research. To this end, the attending physician responsible for the fertility treatment and the researcher or investigator deriving and/or proposing to utilize human pluripotent stem cells should not have been one and the same person.

iii. To ensure that human embryos donated for research were in excess of the clinical need of the individuals seeking fertility treatment and to allow potential donors time between the creation of the embryos for fertility treatment and the decision to donate for research purposes, only frozen human embryos should have been used to derive human embryonic stem cells. In addition, individuals undergoing fertility treatment should have been approached about consent for donation of human embryos to derive pluripotent stem cells only at the time of deciding the disposition of embryos in excess of the clinical need.

iv. Donation of human embryos should have been made without any restriction or direction regarding the individual(s) who may be the recipients of transplantation of the cells derived from the human pluripotent stem cells.

v. Informed consent should have been obtained from individuals who have sought fertility treatment and who elect to donate human embryos in excess of clinical need for human embryonic stem cell research purposes. The informed consent process should have included discussion of the following information with potential donors, pertinent to making the decision whether or not to donate their embryos for research purposes.

21. Informed consent should have included:

i. A statement that the embryos will be used to derive human pluripotent stem cells for research that may include human transplantation research;

ii. A statement that the donation is made without any restriction or direction regarding the individual(s) who may be the recipient(s) of transplantation of the cells derived from the embryo;

iii. A statement as to whether or not information that could identify the donors of the embryos, directly or through identifiers linked to the donors, will be removed prior to the derivation or the use of human pluripotent stem cells;

iv. A statement that derived cells and/or cell lines may be kept for many years;

v. Disclosure of the possibility that the results of research on the human pluripotent stem cells may have commercial potential, and a statement that the donor will not receive financial or any other benefits from any such future commercial development;

vi. A statement that the research is not intended to provide direct medical benefit to the donor; and

vii. A statement that embryos donated will not be transferred to a woman's uterus and will not survive the human pluripotent stem cell derivation process.

22. Derivation protocols should have been approved by an Institutional Review Board (IRB) established in accordance with NIH or FDA regulations. The conditions for the derivation and utilization of ES cells from human **fetuses** set out by NIH are described below.

23. As a policy matter, deriving or utilizing human pluripotent stem cells from fetal tissue should comply with the informed consent law applicable to fetal tissue transplantation research together with the following conditions. The informed consent process should have included discussion of the following information with potential donors, pertinent to making the decision whether to donate fetal tissue for research purposes.

24. Informed consent should have included:
    i. A statement that fetal tissue will be used to derive human pluripotent stem cells for research that may include human transplantation research;
    ii. A statement that the donation is made without any restriction or direction regarding the individual(s) who may be the recipient(s) of transplantation of the cells derived from the fetal tissue;
    iii. A statement as to whether or not information that could identify the donors of the fetal tissue, directly or through identifiers linked to the donors, will be removed prior to the derivation or the use of human pluripotent stem cells;
    iv. A statement that derived cells and/or cell lines may be kept for many years;
    v. Disclosure of the possibility that the results of research on the human pluripotent stem cells may have commercial potential, and a statement that the donor will not receive financial or any other benefits from any such future commercial development; and
    vi. A statement that the research is not intended to provide direct medical benefit to the donor.

Financial issues

25. As suggested in the NIH guidelines this committee agrees that monetary inducement for the donation of human embryos or fetuses for research must be prohibited. The only payment that can be proposed should be one that does not exceed the reasonable costs associated with the transportation, processing, preservation, quality control and storage of ES cells. In order to scale-up and direct the ES cells as fast as possible for therapeutic purposes the results of ES cell research may have commercial potential and must therefore be allowed.

Identifiers

26. If identifiers were to be removed ES cell investigators would not be able to conduct certain genetic studies or develop therapeutic materials. Thus, as recommended in the NIH guidelines, the term 'identifier' should refer to any information from which the donor can be identified, directly or through identifiers linked to the donors. Furthermore since information identifying the donor may be necessary if the derived tissues or cells are to be used in transplantation, it is necessary to state that the informed consent should notify donors whether or not identifiers will be retained. Since ES-derived tissues (heart, nerve, blood etc) will be the best match for the donor supplying the embryos for ES cell derivation, the donor should not be given privilege in the fruits of the successful research either by getting preferential treatment, payments or any other benefits. DNA could also be an identifier and as such all donors of human embryos or fetal tissue should be told that identifiers such as DNA will be retained with the samples. Although DNA can be used to determine an individual from whom a tissue sample was taken, this can be done only when one has a sample from both the tissue in question and the putative donor. It cannot be used to identify an individual out of a population.

Rights, duties and responsibilities of those handling stem cells for research

27. The following actions may be taken by the awarding agency funding the research. Firstly, compliance to certain guidelines (eg. NIH) can be largely determined prior to the award of funds. Regular progress reports could be requested so as to monitor the research. If necessary the awarding agency can impose special conditions on the award including increased

oversight/monitoring/reporting requirements for an institution, project or investigator. If an awardee fails to comply with the terms and conditions of the award, the awarding agency may withhold funds pending correction of the problem or, for more severe enforcement, disallow all or part of the costs of the activity that was not in compliance, withhold further awards for the project, or suspend/terminate all or part of the funding for the project. Individuals or institutions may be debarred from eligibility for all government financial assistance in the future. Harsher punishments than those suggested above will only discourage scientists from getting involved in potential curative stem cell research.

ES Cells and therapeutic cloning

28. Cloning or 'nuclear transfer' in general is of two types viz., reproductive and therapeutic cloning. The process in producing a clone in both cases is the same (generation of an embryo by electric pulse after transplanting any cell with 46 chromosomes into an enucleated human or animal egg). The difference lies in the use put to the generated embryo. In reproductive cloning, the resulting embryo is transferred to the uterus of a woman to deliver a baby. It is important to note that the development of animal reproductive cloning todate has shown a widespread pattern of problems in pregnancy, foetal abnormalities and early deaths of newborn animals. Animal reproductive cloning was strongly criticized in a recent report where it was stated that there is no such thing as a normal clone. Around 75% of cloned cows die in the first two months of pregnancy and miscarriages go on right to the end (Cohen and Concar, 2001). Thus, it has been stated as to why would anyone in their right mind want to clone a human being when animal cloning can go disastrously wrong. This therefore makes it quite clear that for the foreseeable future it would be criminally foolhardy to attempt to clone human beings quite apart from the very strong ethical objections (Bruce, 2001). Thus, this committee recommends very strong objections to producing embryos genetically identical to another human being (reproductive cloning).

29. In therapeutic cloning, ES cells can be derived from the nuclear transferred embryo and these cells can be directed into useful cells and tissues that will

benefit mankind. One advantage of deriving differentiated cells from nuclear transferred ES cell lines is that the transplanted cells may not be rejected because the genome of the donor cell used for the nuclear transfer comes from the recipient. However, the major obstacle to therapeutic applications is obtaining stem cells for every given patient. The second limitation is the recent evidence suggesting that the efficiency of producing nuclear transferred ES cell lines was very low (8.8%). In this study using the mouse model, the authors obtained 398 blastocysts from 1016 reconstructed eggs (39.2%) using tail-tip and cumulus cells. From these 398 blastocysts only 35 cell lines (8.8%) were developed. (Wakayama et al 2001).

30. It would seem illogical to disallow the creation of embryos for stem cell research through in vitro fertilization clinics and at the same time allow the creation of therapeutically cloned embryos for ES cell research. The use of frozen spare embryos from fertility treatments would be a use of an embryo that would be disposed of anyway. Thus, the deliberate creation of human embryos for research via any means must be disallowed. Once therapeutic cloning is allowed it would be easy for someone misguided enough to get to the next step and allow them to be implanted to produce a fully cloned human being. The US congress under the Bush Jr administration recently banned federal and private funding for therapeutic cloning research (NIH, June 2001). Interestingly, guidelines proposed recently allowed Canadian scientists to derive stem cells from human embryos left over from fertility treatments or fetal tissue obtained from elective abortions. However, the 10 member Canadian panel opposed the donation or sale of sperm or eggs to create embryos for the sole purpose of generating stem cell lines. It also urged a moratorium on creating human embryos by therapeutic cloning stating that the underlying science was flimsy and that the practice would inevitably lead down a slippery slope to human cloning (Kondro, 2001). Very recently, Germany also paved the way allowing researchers to import ES cell lines from other countries for research. However, the creation of human embryos solely for research as well as therapeutic cloning was disallowed (Steghauss – Kovacs, 2001).

Cross-species hybrid cells

31. One speculative means to the same end as therapeutic cloning is to produce non-viable human embryos within cow eggs for ES cell research. The concept is the same as nuclear transfer except that the donor human cell is introduced into an enucleated cow egg instead of a human egg. Although theoretically feasible, one would have to be quite sure that the use of the animal egg as a host for the human cell has no adverse effect on the eventual human cell lines. Even though it would avoid the creation of a viable human embryo, the mixing of human and animal genetic material at such a profound level would raise major clinical and ethical objection by most people. Thus, cross-species experimentation must be strongly discouraged.

What happens once a HES cell line has been established?

32. Once an ES cell line is established the cells can go on proliferating forever in an undifferentiated state and can be made immortal. Thus the need for more embryos or cell lines is not necessary. A few cell lines are adequate for the whole world. At any stage of proliferation if a single ES cell is transferred to the uterus of a woman, it cannot develop into a complete human being. If transferred in large numbers into the human body without directed differentiation there is the risk of producing teratomas (tumours). Thus it is imperative that ES cells be first directed into specific cell types and tested in animal models before transplantation into humans.

33. Once ES-cell derived heart, nerve, blood etc cell types have been produced, their usefulness in curing disease though transplantation therapy should first be tested on laboratory and larger animal models before direct human transplantation. For this reason therefore transfer of human ES-derived cells to animals (xenografting) to ensure safety and efficacy must be allowed. Thus xenotransplantation of human ES derived cells to specific laboratory and large animals such as mice, rats, primates and pigs must be permitted for reasons of convenient testing, accurate assessment of functional clinical outcome, genetic closeness to the human and histocompatability. For research, the ES or ES-derived cells should not be sold to other researchers but instead distributed free so as to expedite the clinical benefits to mankind as soon as possible.

Clinical trials

34. The same regulations governing any clinical trial should be applied to ES-derived cells. Before applying such cells in the human, these newly derived cells must be screened for microbes and safety. There must be adequate counseling, informed consent, privacy and confidentiality regarding the clinical application. The participants should not be entitled to any benefits or share in the fruits of success of the clinical trial. The possible cure of the specific illness in itself is a benefit. During the counseling process, the participant should be informed that the procedure is at his/her own risk and there would be no compensation for such risks.

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ETHICAL CONSIDERATIONS IN STEM CELL RESEARCH

General remarks

1. The entire field of biomedical research and technique is changing very fast. It is therefore necessary to try and find basic or fundamental principles that apply generally, and to avoid a situation where ad hoc rules are set up only to be quickly overtaken by further developments.

2. Stem cell research includes both theoretical (or basic) and applied (or practical) aspects. The main intended benefits are:

   a) Theoretically, advancing understanding of tissue differentiation, development, repair and ageing.
   b) Practically, the therapeutic use of undifferentiated tissue for organ/tissue replacement or repair.

3. The distinction between theoretical and applied research, in any field, is one of time scale. In the long run, theoretical advances find application. In the short term, research can address immediate problems. Others problems may arise unanticipated, however. If we knew the outcome of research in advance, we would not have to do it in the first place. Therefore, the benefits of research, like its results, cannot be completely specified in advance. The costs, similarly, cannot always be foreseen. Such costs may include ethical and social costs.

4. Ethical and social issues arise to some extent whenever scientific research is carried out, because the outcome affects people. In particular, such issues arise in biomedical research because the interests of potential beneficiaries may compete with, and may have to be considered together with costs to society or to other individuals, such as donors. There are relatively clear-cut guidelines on research ethics available elsewhere, e.g. US NIH guidelines on research on human embryonic stem cells.

5. Medical practitioners have obligations to individual patients, and therapeutic or preventive application of research findings has to be moderated on a case by case basis, such that there is a clear and identifiable benefit and no important general principle is contravened.

6. Then boundary between therapeutic, preventive, and non-therapeutic intervention is difficult to mark clearly. For example, the principle of intervention to improve on natural genetic endowment would seem to have been established by some uses of cosmetic plastic surgery (for example, breast enhancement). Similarly, recourse to abortion as a method of family planning is only loosely therapeutic, (on the argument that proceeding to term jeopardises the mother's mental state) and is primarily a quality of life issue.

7. Stem cell research raises a number of such issues, which seem to fall naturally into two groups:

a) Issues surrounding the origins of stem cells, in particular, the use of embryo stem cells. Even if it is assumed or determined that the source embryos would never have been enabled to develop as individuals, the use of such tissues does raise assumptions about the status of embryos which have to be addressed. Similarly any claim that no further recourse to embryos is needed does not remove the obligation to address the issues, since the need may still recur. In any event moral principles have retrospective application, though the passage of time may blunt their urgency in particular cases.

b) Issues relating to the use of stem cell tissue. In general the issues are similar to those relating to organ donation and focus on the need for appropriate regulation.

8. Stem cell research also prompts consideration of the potential non-therapeutic use of biomedical techniques, which might also include cloning, genetic modification, and artificial fertilization. These techniques allow the power to intervene actively in the physical creation, maintenance, alteration or repair of humans. In so doing they call into question many of the conventional assumptions about the propriety of interfering with the creation or modification of people. They may also be seen as threatening the conventional structure of families.

9. It should be noted that these ethical issues do not hinge upon a distinction between what is natural and what is not. There is no necessary convergence between what is natural and what is best, though there may be (for example, in recommending mothers to breast feed). In its entirety, medical science is concerned with interventions, whether preventive, therapeutic, surgical, emergency, or aimed at improving quality of life and recommending healthy lifestyle choices. In this sense, it is never natural, though it is ultimately based on the scientific study of natural biological phenomena.

10. The issues raised in 7 and 8 above are considered in more detail in the following sections.

The origins of stem cells and the use of embryos

11. Stem cells may come from the sacrifice of embryos, or from adults in the form of umbilical cord or bone marrow tissue donations. There is some difference of opinion as to the merits and potential of stem cell lines from these respective sources, and the extent of likely future requirements for embryos. Balance of opinion appears to be that embryo stem cells have greater potence and potential for therapeutic use than adult cells. However, the ethical issues need to be considered anyway.

12. As regards adult sources of stem cells the sourcing is not very controversial and is considered under the issue of regulation.

13. Acceptability of the use of human embryo tissue for stem cell supply is more controversial. Such use raises ethical issues centred on the question of whether or not human embryos can be regarded as disposable for benevolent

purposes. An embryo used for the sake of its stem cell tissue is not able to develop to term, and a potential human being is denied existence. Regularising the use of embryos in this way in effect devalues their future human potential in favour of their immediate value as a source of tissue. This is not necessarily an unjustifiable priority, since no realistic possibility of development may ever have existed, but it certainly needs to be examined. The extent to which an embryo should be regarded as having a right to life is disputed and raises strong views, even though an embryo is by definition not a foetus.

14. Reasons for suggesting that it is acceptable or actually morally desirable to use embryo tissue hinge on arguments that propose that the embryo (as distinct from the foetus), is not entitled to full human status, plus arguments to the effect that the embryos which may be used in stem cell research would never in any event have developed as people. Specifically it can be argued that :

a) An embryo is only a potential foetus. It has undifferentiated tissues and its form and stage of development are not yet recognisably human. It has no differentiated nervous tissue and so cannot feel pain.
b) A potential foetus and an actual human should not stand in a relation of equality where human rights are concerned. The needs of adult humans or children deserve more consideration than the needs of embryos, where there is a conflict. This is because adults or children carry an investment of experience (realised potential) and are self-aware.
c) By extension of (b) it could paradoxically diminish respect for human life to extend the rights and privileges of an adult human to an insentient embryo and treat them as equivalent. It could be seen as implying that awareness and sentience entail no corresponding consideration.
d) Embryos available as a source of stem cells are in practice those that would in any event not have been allowed to develop to term, having been engendered for other purposes such as fertility treatments.
e) It is morally objectionable to deny people the benefits of embryo stem cells if (a) to (d) above are accepted. There is ample precedent for sacrificing foetuses in abortions, so an embryo, which is the precursor to a foetus, cannot rationally enjoy a more privileged position if the benefits are deemed as great or greater.
f) The requirement for further embryos may be very modest.
g) Creation of embryos specifically for stem cell tissue might be deemed justifiable under (a) to (c) above, but practically speaking it is preferable to outlaw this practice on the utilitarian grounds that the less respect for human life is apparently called in question in the use of embryo stem cells, the better. Moreover, there are objections to reproductive cloning of embryos (see below). It might be useful occasionally to create an embryo for therapeutic cloning, i.e. as a source of stem cells genetically identical to the anticipated host. However, to eliminate the danger of facilitating an illegitimate reproductive cloning attempt, it might be wiser to simply outlaw all cloning.

15. However, the arguments set out above will not satisfy those who maintain that from the moment of conception an embryo is a human being and should be treated accordingly. Arguments for according full human status for embryos can be summarised as follows:

a) It diminishes respect for human life not to treat embryos as de facto humans, the arguments above notwithstanding.
b) By extension of (a), once a decision is made to deny human status in principle to embryos, a precedent will have been set which may extended to other categories of human beings such as the profoundly disabled or the elderly infirm.
c) Using embryo tissues conflicts with some religious convictions.

16. This particular issue is not one that is likely to be rationally resolved to the satisfaction of all parties, because the commitments to positions are often driven by moral or religious conviction. However, the following considerations seem salient from the point of view of developing a policy:

a) Singapore is a secular state, and in the interests of religious tolerance and social harmony specific religious convictions cannot be the basis for determining policy. However, no-one should be compelled to act contrary to their religious or moral convictions. Therefore, if an embryo is to be used in stem cell research, it cannot be in contradiction to an expressed religious or conscientious objection by persons in loco parentis, if any.
b) Similarly, no person should be compelled to destroy or help destroy an embryo in contradiction to religious conviction.
c) There is already established legal and medical precedent in Singapore that a foetus does not in all circumstances enjoy the rights of a post-partum child.
d) The line between an embryo and a foetus is not arbitrary.
e) The argument that respect for the disabled or elderly infirm will be undermined by regarding embryos as expendable in some circumstances might be mitigated by recognition that a potential benefit of stem cell research is the means to assist these very groups. It is arguable that respect for life actually benefits from the appropriate and controlled use of embryo stem cells.
f) Sources that rely on the principle of voluntary donation by informed consent of adult donors are preferable to sources that rely on termination of embryo potential, all else equal.

17. Two fallacious arguments may be mentioned:

a) Many embryos spontaneously abort anyway, so it is acceptable to utilise embryos in research. The fact that something is frequent does not mean it is acceptable; moreover, spontaneous abortions may reflect biological unviability of particular embryos, and cannot be a ground for asserting the general expendability of embryos.
b) Destroying an embryo might be destroying a potential genius. This argument is sometimes produced in debates over abortion, but it is

fallacious on two grounds. It is selective (it overlooks the fact that one might as easily be destroying a potential retardate), and it is inequitable (implicitly asserts a greater moral right to life of a particular class of people, viz., potential geniuses).

18. The importance of respect for human life is not in question, but it is best expressed by regulating, not prohibiting, the use of embryos.

Issues relating to the use of stem cell tissue.

19. Normally the keeping or disposal of human organs or tissue is treated with respect or even reverence, because it is a part of some individual person, or even a complete person, and because it is normally evidence of death. The exception is when organs or tissues are donated. A stock of stem cell tissue has somewhat the character of a stock of blood in a blood bank. Taken together, developments in transplant technology and stem cell research might be held to undermine the idea that there is anything special about human tissue per se. Rather, it supports thee view that tissue is quite separate from the individuals whom it comprises. This argument is developed in 20-23 below.

20. Over time, the constituent cells of the body, other than neurons, replace themselves. Even neurons, however, grow and alter their synaptic connections. These facts make it impossible to reduce an individual's identity to a collection of tissues, because these tissues change over time though the person they instantiate does not. People are therefore defined by the integrated action of their tissues.

21. If the function of a tissue is maintained, its physical embodiment can change without prejudice to the integrity of the person as a whole. Some, in defining a person, would wish to argue an additional immaterial but essential constituent such as a soul or a mind. Others of a more materialist persuasion might feel that we have no need for recourse beyond the fully functioning brain to account for individuality. In either case, however, there would be wide agreement that integrated functioning is important for a coherent person to exist, i.e. that it is the nature of the system as a whole and not merely its parts that is important. This reflects a shift from structure to function as the defining mark of a person.

22. If this is granted, it follows that tissue derived from stem cells can be used to repair or construct body organs, as can artificial materials, without any ethical complications arising from an unnecessary sense of residual ownership. For example, if animal tissues, say, or artificial hearts, or synthetic blood, functioned equivalently to the corresponding natural human article, they could be used in therapeutic ways without incurring any ethical dilemmas. Tissues are just tissues.

23. Clearly some implications of this dissociation of tissues from people as individuals could offend taste or religious belief. For example, many people

might find the idea of animal tissues or organ transplants distasteful, or in some cases prohibited by their religions, but taste and prohibitions are not ethical issues. Treatment is voluntary and no-one need undergo a procedure they find unacceptable. Tissue donation and organ transplants have been generally recognised as acceptable. The exceptions tend to be belief systems generally hostile to medical or surgical interventions, preferring in principle other forms of therapeutic intervention, or none. No-one, however, is compelled to accept medical or surgical interventions, and debate tends to arise only over in the case of minors, where the beliefs of parents or guardians can conflict with the rights of minors as recognised in law.

24. A further implication is that an individual does not retain ownership of tissue once donated, nor do they have any unique claim on the benefits of research. This does not preclude arrangements analogous to autologous blood donations in any situation in which stem cells could appropriately be maintained for the benefit of the donating individual.

25. Examples of acceptable donations and their ethical justification include:

a) Blood donation: immediate saving of life, minimal risk to donor.
b) Bone marrow transplants: long term saving of life or delaying death. Slight operative risk to donor.
c) Kidney donation: long term saving of life, sparing the expense and inconvenience of dialysis; some operative risk to donor and recipient, and long term loss of reserve function in donor, who has to rely on a single remaining kidney.
d) Organs donated upon death of the donor: long term saving of life at no cost to the donor; some potential pain or distress to relatives in the process of securing permission where required (i.e. other than under prearranged donation schemes), or where relatives may object to donation for their own reasons irrespective of the donor's wishes.

26. The ethical principles that apply in cases like this can be summarised as follows:

a) Donor choice. People are free to donate tissue or organs. However, as there may be a risk to the donor, this choice should be one made freely. For this reason donations are not acceptable where there is a conflict of interest such that a donor might feel impelled to donate despite a health disadvantage. Examples arise when tissue or organs are sold, or donated for a consideration. Only autologous or unpaid anonymous donations avoid this problem.
b) Donor information. It is necessary that donors be clear, and if necessary reassured, as to the scope and limitations of use of donated tissue, including their agreement to relinquish rights over the tissue and the research or treatments that use it, which have to be determined by research and clinical criteria.
c) Donor competence. When the donor is incompetent, being dead, or not of sound mind, decisions have to be made by proxy. The default is that

donation does not occur unless the law provides for an alternative default or other provisions have been made.

27. The donation of stem cell tissue by consenting informed adult donors, whether for research or therapeutic purposes, does not seem to raise additional ethical issues per se, over and above those inherent in donation generally. The risks are low, or non-existent.

28. In general, therefore, the issues of regulation appear very much capable of accommodation within the rules applicable to organs, and there need be no qualms about research with, or therapeutic use of, adult stem cell tissues.

Non-therapeutic use of biomedical techniques

29. Emerging biotechnologies, including stem cell research, offer the potential for proactive use of technology to actually design or improve humans, as opposed to therapeutic uses that correct defects, repair injuries, or cure diseases. This implies a great increase in the control that can be exerted over people and society. How then is this control to itself be regulated? This is the concern that lies behind the catchphrase 'playing God'. It may be noted that the concern is over the design. For example, we at present grant parents more or less unlimited rights to produce accidental children by unassisted natural reproductive processes.

30. To illustrate the problems raised by proactive genetic engineering consider the following hypothetical scenario. If we could in fact freely specify the genotype - as affecting characteristics, personality, ability, physical form and gender of our infants - what restrictions would we want to put upon that choice, and how administer them? If we take a time frame of, say, 20 years, it is by no means clear that this scenario is entirely hypothetical. However, it is instructive to try and imagine, given relatively unlimited power of design, the ways in which we might then see reasons to curb it.

For example:

a) Possibility of choice raises the possibility of losing it and substituting totalitarian control.
b) The interests of parents may conflict with each other, or their children, or state interests (e.g. gender choices under a one child policy).
c) Ignorance of pleiotropic genetic effects or interactions might subvert good intentions.
d) It undermines the notion of individual autonomy to (in effect) create designer children, because the designer (parent, doctor, etc.) carries the responsibility for the kind of person created.
e) The intentions of parties may not necessarily be benevolent.
f) Insofar as an argument from what is natural has any force, it has force in arguing for a conservative approach to engineered change, because human nature, being a product of evolutionary pressures, is an

integrated whole. Piecemeal 'improvement' may prove undesirable in the long run in unforeseen ways.

g) Those who reject an evolutionary approach for religious reasons would however see engineered change as ethically objectionable or even blasphemous because it usurped the role of the creator.

31. Examples of potential active interventions designed to improve and design people might include

a) Selecting or creating foetuses with favourable genetic characteristics or of a desired gender (as against aborting or discarding those with unfavourable characteristics, actual genetic defects, or of undesired gender).
b) Attempting or planning to clone children (the nearest equivalent being the natural occurrence of monozygotic twins).
c) Delaying the implantation/birth of a twin to optimise child-rearing (for example, by spacing out children, or in order to gain the experience of difficulties facing the first twin which could then be anticipated in a second identical sibling).
d) Using stem cell tissue for organ improvement (as against therapeutic replacement or repair).

32. Such possibilities would be controversial precisely because they actively go beyond the therapeutic and remedial. As long as medical science was essentially remedial, it enjoyed an accepted ethical position embodied in the Hippocratic oath (cure your patients, do no harm, keep secrets). Once it became possible to go beyond therapy, other issues were raised. Even within therapeutic medicine and surgery there are of course many ethical issues, for example those surrounding consent with children or assisted death, but new ones are raised by new technologies which allow, in effect, a eugenic or design component.

33. In addition, human societies in general, and certainly in Singapore, take the family unit as core to society as we know it or wish it to be, and techniques that seem to affect or undermine the norm of the family are apt to be found objectionable. It is where families are concerned that the idea of a natural way of doing things has its greatest appeal. Much of the resistance to alternative family arrangements, such as same sex marriages or voluntary single parenthood, extends also to biomedical techniques that extend the frontiers of what might be possible. Thus, questions arise if, for example, post-menopausal mothers seek to bear children, or parents seek to take action to replace a lost child with another of the same sex, or with a cloned offspring. In the normal way of things, parents have no say in determining the genotype of their offspring. A cloned or genetically modified individual, however, is beholden to his or her creators/modifiers for specific characteristics. This obligation is different from and somewhat beyond the normal family obligations of a natural child. In a very definite sense a designed child therefore less an autonomous or unique individual. The possibility of invidious comparisons also arises once the possibility of an element of 'design' is introduced.

34. This point needs elaboration. Once it becomes possible to create or modify individuals, the concern arises that those who are less favoured may feel more discriminated against or made to feel excluded more than they otherwise would, because of the implication that imperfection could have been avoided, and that someone is culpable. This is a known effect in certain conditions, such as dyslexia, schizophrenia and autism, where for many years parents were made to feel guilty and children inadequate, because it was believed, in some quarters, that these conditions were a result of inadequate instruction or parenting. The acceptance of dyslexia as having a neuropsychological basis removed this guilt; the idea of the 'schizophrenogenic mother' is not now widespread; and autistic children are no longer regarded as the product of aloof and detached parents. However, some of this guilt might be restored if it became possible to avoid dyslexia, or schizophrenia, or autism, by suitable genetic engineering or by choice of embryos. A similar argument extends by analogy to any mental or physical condition such as intelligence or looks, where an element of genetic modification is possible.

35. The general claim is therefore that the unpredictability of the individual genome is critical to preservation of individuality.

36. It would seem therefore, that considerations such as those under 30-35 above should lead to a reluctance to countenance proactive non-therapeutic interventions and eugenic trends generally.

Conclusion

37. Given that stem cell research is likely to yield benefits for organ and tissue repair and replacement, the ethical issues it raises are those of supply and regulation. In the actual use of stem cell tissue in this way there is no general ethical objection. The issue of obtaining embryo stem cells is ethically resolvable.

38. When active non-therapeutic techniques are considered, including techniques using stem cells, a conservative position is recommended, since there are a number of reasons for caution, especially ignorance of the consequences and concerns as to the implications for individual integrity.

Issues raised by the Bioethics Advisory Committee

39. BAC 1. The potential benefits do seem to justify stem cell research, because

    a) There is obvious benefit in exploring ways in which tissues or organs might be repaired using non-differentiated tissue. The entire principle of using tissue in this way is a new one, and while it is too soon to know the limits of what will prove possible, there can be little doubt but that the possibilities ought to be pursued.
    b) The benefits and outcomes of research cannot be fully specified in advance.

40. BAC 2. The merits of embryonic stem cells over other stem cells are debated, but there are grounds for arguing that they have the greatest pluripotency and are in general preferable to cells from other sources. The concerns over sacrificing embryos are not sufficient to outweigh this merit.

41. BAC 3. It is hard to argue for a restriction on stem cell research to areas with a high level of benefit. This is an issue of prioritisation in research, and priority in funding and support might be given to areas likely to show the greatest benefit. However, the uncertainty of the research enterprise is such that rather than restrict it, a policy of selective prioritisation might be more appropriate. There are no ethical reasons for an actual prohibition on research in advance. Individual research proposals will in any case need to be considered by ethics committees which will take into account both the details for the proposed procedures and its likely theoretical or practical benefit.

42. BAC 4. Clear guidelines exist elsewhere for informed consent, and should be adopted in Singapore also. In general, however, the donation of stem cells should not be linked to financial benefits or benefits in treatment.

43. BAC 5. A code of conduct analogous to those governing the management of donated organs or tissues generally will be needed.

44. BAC 6. It is argued that it is ethically acceptable to utilise embryos. It is probably neither necessary not desirable to create embryos for research or as a source of stem cells. It might be ethically justifiable to do so should the need exist, but in practice the need can apparently be met from embryos or foetuses incidental to other procedures such as abortion or fertility treatment, and there need be no ethical objection to their use for research. Specifically,

    a) Ethically, stem cells from aborted foetuses could be used, but practically are not an ideal source.
    b) Embryos from fertility treatment can ethically be used whenever there is no prospect of such embryo ever developing to term.
    c) It should not be necessary to create embryos for research in vitro.
    d) In theory, therapeutic cloning is ethically acceptable, but in practice it might be wiser to ban it.
    e) Reproductive cloning should certainly be disallowed
    f) Sale and commercial supply of embryos should be disallowed.

45. BAC 7.
    a) Xenografting and xenotransplantation raise no unique ethical problems so long as the principle of voluntary agreement to treatment is observed. There need be no objection in principle to research in this area.
    b) Sale and commercial supply of stem cells should preferably be disallowed, in favour of some system of distribution that recognises and evaluates the clinical and research intentions of prospective users

46. BAC 8. It is difficult to see specific ethical objections to cross-species experimentation per se. However, there is widespread public concern over issues of genetic modification generally. It would be advisable to limit cross-species experimentation except in cases where a clear anticipated benefit is unattainable by other means.

47. BAC 9. The issues raised regarding trials appear no different from those in other areas of research. For example, the extent to which trials might need to be conducted on animals or humans is determined by the need for reasonable certainty as to the safety and efficacy of a procedure.

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SOMATIC CELL NUCLEAR TRANSFER (CLONING) - SCIENCE

Introduction

1. Nuclear transfer involves transferring the nucleus from a diploid cell (containing 30-40,000 genes and a full set of paired chromosomes) to an unfertilised oocyte from which its chromosomes have been removed. The technique involves several steps: synchronization of the donor nucleus into G0 phase of its cell cycle; transfer into an "enucleated" oocyte; fusion of the 2 cells; activation of the "hybrid" cell; and growth of the cell into an embryo. The nucleus itself can be placed into the peri-vitelline space of the oocyte or the intact cell can be injected directly into the oocyte. In the former case, the oocyte and donor cell are normally fused and the 'reconstructed embryo' activated by a short electrical pulse. In the sheep (as with Dolly), the embryos are then cultured for 5-6 days and those that appear to be developing normally (usually about 10%) are implanted into foster mothers.

2. Nuclear transfer is not a new technique. It was first used in 1952 to study early development in frogs and in the 1980's the technique was used to clone cattle and sheep using cells taken directly from early embryos. In 1995, Ian Wilmut, Keith Campbell and colleagues created live lambs - Megan and Morag - from embryo derived cells that had been cultured in the laboratory for several weeks. This was the first time live animals had been derived from cultured cells and their success opened up the possibility of introducing much more precise genetic modifications into farm animals.

3. In 1996, Roslin Institute and PPL Therapeutics created Dolly, the first animal cloned from a differentiated somatic cell taken from an adult animal (Wilmut et al, 1997). In August 1998, Wakayama et al published a report of the cloning of over 50 mice by nuclear transfer. Since then, the cloning of cattle, sheep, mice, goats and pigs have been reported, but not for rabbits, rats, monkeys, cats or dogs.

4. There are differences in early development between species that might influence success rate. In sheep and humans, the embryo divides to between the 8- and 16-cell stage before nuclear genes ("genomic activation") take control of

development, but in mice this genomic activation occurs at the 2 cell stage. In 1998, a Korean group claimed that they had cloned a human embryo by nuclear transfer but their experiment was terminated at the 4-cell stage and so they had no evidence of successful reprogramming; there was no publication.

5. Currently, success rates remain very low in all species, with published data showing that on average only about 1% of 'reconstructed embryos' leading to live births. Many cloned offspring die late in pregnancy or soon after birth, often through respiratory or cardiovascular problems. Abnormal development of the placenta is also common and this is probably the major cause of fetal loss earlier in pregnancy. Many of the cloned cattle and sheep that are born are much larger than normal ("large fetus syndrome"). The high incidence of abnormalities is not surprising. Normal development of an embryo is dependent on the methylation state of the DNA contributed by the sperm and egg, and on the appropriate reconfiguration of the chromatin structure after fertilization. Somatic cells have very different chromatin structure to sperm and 'reprogramming' of the transferred nuclei must occur within a few hours of activation of reconstructed embryos. Incomplete or inappropriate reprogramming will lead to dysregulation of gene expression and failure of the embryo or fetus to develop normally or to non-fatal developmental abnormalities in those that survive.

6. A major effort is now being made to identify systematic ways of improving reprogramming, through: (1) known mechanisms involved in early development, and in particular on the 'imprinting' of genes; (2) technological advances in genomics to screen the expression patterns of genes to identify differences between the development of 'reconstructed embryos' and those produced by in vivo or in vitro fertilization.

Applications of SCNT

i. Cloning in Farm Animal production

7. Nuclear transfer can in principle be used to create an infinite number of clones of the very best farm animals. In practice, cloning would be limited to cattle and pigs because it is only in these species that the benefits might justify the costs. Cloned elite cows have already been sold at auction for over $40,000 each in the

US but these prices reflect their novelty value rather than their economic worth. To be effective, cloning would have to be integrated systematically into breeding programmes and care would be needed to preserve genetic diversity. It would also remains to be shown that clones do consistently deliver the expected commercial performance and are healthy and that the technology can be applied without compromising animal welfare.

ii. Production of Human Proteins for Therapy

8. Human proteins are in great demand for the treatment of a variety of diseases. Whereas some can be purified from blood, this is expensive and runs the risk of contamination by HIV or Hepatitis C. Proteins can be produced in human cell culture but costs are very high and output small. Much larger quantities can be produced in bacteria or yeast but the proteins produced can be difficult to purify and they lack the appropriate post-translational modifications that are needed for efficacy in vivo.

9. By contrast, human proteins that have appropriate post-translational modifications can be produced in the milk of transgenic sheep, goats and cattle. Output can be as high as 40 g per litre of milk and costs are relatively low. PPL Therapeutics has produced alpha-1-antitrypsin through such an approach, and this protein is due to enter phase 3 clinical trials for treatment of cystic fibrosis and emphysema in 2001. Nuclear transfer allows human genes to be inserted at specific points in the genome, improving the reliability of their expression and allows genes to be deleted or substitutes as well as added.

iii. Xenotransplantation

10. The chronic shortage of organs means that only a fraction of patients who could benefit actually receive transplants. Genetically modified pigs are being develop as an alternative source of organs by a number of companies, though so far the modifications have been limited to adding genes. Nuclear transfer will allow genes to be deleted from pigs and much attention is being directed to eliminating the alpha-galactosyl transferase gene. This codes for an enzyme that creates carbohydrate groups which are attached to pig tissues and which would be

largely responsible for the immediate rejection of an organ from a normal pig by a human patient.

iv. Cell Based Therapies

11. Cell transplants are being developed for a wide variety of common diseases, including Parkinson's Diseases, heart attack, stroke and diabetes. Transplanted cells are as likely to be rejected as organs but this problem could be avoided if the type of cells needed could be derived from the patients themselves. The cloning of adult animals from a variety of cell types shows that the egg and early embryo have the capability of 'reprogramming' even fully differentiated cells. Understanding more about the mechanisms involved may allow us to find alternative approaches to 'reprogramming' a patient's own cells without creating (and destroying) human embryos.

12. With such cells, the potential in clinical use will include the following:
    a) Replacement tissues & organs;
    b) Prevention of immunological tissue rejection;
    c) Enhancement of immunological survellance; and
    d) Gene therapy

13. The implications of such clinical applications include the ability to treat and overcome aging, disease, cancers, myocardial infarctions, renal failure, liver failure, and genetic disorders.

14. These cells will form the basis of new therapies in the battle against death and disease – cell-based therapies will be the next major approach in medicine. The simplest approach is to seed satellite cell clusters of healthy donor progenitor cells in a diseased or dysfunctioning organ, and this may be all that is necessary. The next level is to produce primordial or rudimentary organs with primordial cells which can replace the diseased organ in part or in whole. The final step is to develop the organ completely ex-vivo, probably in conjunction with xenotransplantation, before transplant.

Limitations of nuclear transfer

15. SCNT has many limitations currently, especially its low success rates, but this is due to the infancy of the technique. As basic understanding of this fundamental manipulation improves, success rates will improve.

16. Other requirements for cloning are an appropriate supply of oocytes and surrogate mothers to carry the cloned embryos to term. Use of animal oocytes is an alternative, but this approach poses many questions, both scientific and ethical. In fact, the fusion / introduction of human nuclei into animal oocytes is not permitted in many guidelines related to SCNT.

17. Cloning of endangered species will be possible by using eggs and surrogates from more common breeds of the same species. It may be possible to clone using a closely related species but the chance of successfully carrying a pregnancy to term would be increasingly unlikely if eggs and surrogate mothers are from more distantly related species. Proposals to 'save' the Panda by cloning, for example, would seem to have little or no chance of success because it has no close relatives to supply eggs or carry the cloned embryos.

18. Plans to clone extinct species have attracted a lot of publicity. An Australian project aims to resurrect the 'Tasmanian tiger' by cloning from a specimen that had been preserved in a bottle of alcohol for 153 years. Another research group plans to clone a mammoth from 20,000 year old tissue found in the Siberian permafrost. Unfortunately, the DNA in such samples is likely to be fragmented and the chances of reconstructing a complete genome is highly unlikely. Moreover, nuclear transfer requires an intact nucleus, with functioning chromosomes.

Reproductive and Therapeutic Cloning

19. There are 2 forms of SCNT: reproductive and therapeutic. The former results from replacement of the cloned embryo into a surrogate mother, to allow pregnancy and a live-birth. This approach is important in animal technology and farming, as well as in the pursuit to clone endangered animals. Reproductive cloning of a human is not permitted by many governments and agencies.

20. Therapeutic cloning is the production of cloned cells to produce tissues and/or organs, mainly to improve healthcare treatments. This approach is that taken by many research groups and companies.

21. Because SCNT requires the production of an embryo, the cells produced are completely toti-potent, ie able to produce a complete individual, and that is the basis of reproductive cloning. As the embryo develops further, it is possible to collect only the inner cell mass cells of the embryo (the part of the embryo that forms the fetus and hence all the possible tissues in the body, except the placenta and placental membranes which come from the trophectoderm) and hence embryonic stem cells.

Strategies to produce Stem Cells

22. All cells contain the genetic material and instructions in its DNA to form all the proteins and enzymes in the life of the animal or person from whom it comes. There is now a major research effort in unraveling the time sequence and relational positioning to understand developmental processes. With this understanding and knowledge it will be possible to produce progenitor cells that can develop into specific tissues that are needed.

23. It is now appreciated that adults have stem cells in certain tissues to enable repair and re-population, and that these stem cells can de-differentiate to re-populate tissues of different types. Hence one strategy is to de-differentiate adult stem cells, from tissues that have them in abundance, eg adipose and bone marrow. Because the age of the individual may have a bearing on the telomerase length of the stem cell, it is logical to move to stem cells which can be collected at birth. Umbilical cord stem cells are found in the umbilical cord and the placenta that are usually discarded following the birth of the child. Many institutions are now realizing the potential benefits to collect such cells, which can be stored for the child's own use in the future, or matched for donation if necessary. These cells, obtained from a fully formed individual, though at different ages, are multipotent, in that they can form several types of cells.

24. Another strategy is to go even earlier into a developing embryo or fetus to obtain stem cells that are pluripotent. This has been discussed by Ariff Bongso in his submission.

25. The last strategy is to produce a cell that is completely totipotent, and that can only come from an embryo that is able to produce a complete individual, ie with the cells that can produce the placenta and membranes in addition to the fetus. This is different from embryonic stem cells that can only produce the embryo, and not the placenta. This is achieved through somatic cell nuclear transfer to re-program its nucleus to "go-back" completely to its very first division ("cloning"). The added advantage of this approach is that the genetic material is that of the donor, and hence, there is no ethical repulsion, cf a donated cell / organ, or immunological rejection.

26. The best strategy, with the least controversy, is to re-instruct an adult differentiated somatic cell to form a progenitor cell of a specified tissue type without the need to form an embryo.

Embryonic Stem Cells

27. The source of embryonic stem cells can be classified into 3 main groups: Wild-type ES cells; Genetically-altered ES cells; and ES cells from SCNT.

28. To limit ES cells to a few cell-lines can have major potential repercussions. These ES cells are genetically identical to the donor. Widespread use of these cells would be similar to producing a large number of chimeras with a link to only a few donors; as there is no one without any form of recessive genes, it would be tantamount to allowing widespread propagation of a gene mutation.

29. Another potential problem is the propensity of ES cells to form teratomas; in fact it is this property that characterizes an ES cell. Hence introduction of ES cells which are not properly differentiated into a particularly cell line may result in formation of a tumour (Solter, 1999).

SOMATIC CELL NUCLEAR TRANSFER (CLONING) - ETHICS

30. Many ethical and moral concerns have arisen over the potential applications of the cloning technology. The technology is still in its infancy and in the meantime, society as a whole has time to contemplate which uses of the technology might be acceptable and which would not. It is also impossible to predict all potential applications of a new technology. Most will be beneficial but all technology can be misused in one way or another. The solution is not to regulate the technology itself but how it is applied.

31. There is also concern that scientists are "playing at God". However, mankind has always been altering nature. Animals were first domesticated about 5000 years ago and selective breeding since has produced modern strains of livestock, plants and pets which are very different from their original progenitors. In medicine, our current life expectancy of well over 70 years is a result of direct intervention in nature, from improved prenatal care, vaccination and use of antibiotics. The human condition is still far from perfect and there is no particular reason now to call a general halt to what most people view as progress.

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As this submission is to be part of the deliberations of the Bio-Ethics Advisory Committee on Human Stem Cell Research Sub-Committee, it will be relatively concise.
This submission is based on a review paper in preparation by Ng et al (2001).

PREIMPLANTATION GENETIC DIAGNOSIS

INTRODUCTION

1. Inherited genetic diseases have been a dreaded problem for some families attempting to conceive a child. If affected parents or carriers of genetic disorders wished to avoid transmitting a condition to their child, they can choose to have prenatal diagnosis of their fetus. Amniocentesis or chorionic villus sampling enables cells from the fetus to be collected and sent for genetic analysis. They could then choose to terminate the pregnancy if the fetus is affected.

2. Preimplantation genetic diagnosis (PGD) is the prevention of the birth of affected children in couples at genetic risk by sampling and genetic testing of nuclear material obtained from blastomeres or polar body biopsy of the embryo thus enabling selection and transfer of only normal embryos to achieve a normal pregnancy and birth of a healthy baby. In this way, couples do not have to experience the agony of aborting affected fetuses.

BACKGROUND

3. The first clinical PGD was reported by Handyside and co-workers[1] who described the sexing of preimplantation embryos at risk for sex-linked disease by performing embryo biopsy at the cleavage stage and sexing with Y-specific DNA amplification. A few years later, the introduction of fluorescent in situ hybridization (FISH), a method in which fluorescent labeled, chromosome-specific probes are hybridized to metaphase or interphase chromosomes were reported, allowing sexing of embryos as well as aneuploidy screening[2]. Single gene disorders have been diagnosed with the polymerase chain reaction (PCR). DNA analysis is performed either on biopsied blastomeres or on sampled first and second polar bodies.

BIOPSY METHODS

(i) Polar Body Biopsy

4. The first and second polar bodies contain the complementary genotype to the oocyte. To remove the polar bodies, the oocyte is held with a holding pipette with the polar body at the 12 o'clock position. Using a sharp needle, a slit is made in the zona pellucida tangentially to the polar bodies. With a thin pipette, the polar bodies are removed from under the zona and transferred to a PCR tube or glass slide for analysis.

(ii) Cleavage Stage Biopsy

5. This is the most widely used technique. The advantage of cleavage stage biopsy is that the genetic constitution of the embryo is completely formed and thus

comparable to genetic material obtained at prenatal diagnosis. Embryos are usually obtained after intracytoplasmic sperm injection (ICSI). This avoids contamination with sperm, which is important when PCR is used and reduces the possibility of failure of fertilization with insemination. A hole is made in the zona pellucida of the embryo by applying Acid Tyrode's solution or using a laser. A pipette is inserted through the hole and one blastomere is aspirated and removed from the embryo for analysis. Diagnosing one or two cells isolated from 8-16 cell embryos may occasionally fail to detect mosaicism.

METHODS OF DNA ANALYSIS

(i) In Situ Hybridization

6. In situ hybridization permits the analysis of genetic material of a single nucleus in metaphase or interphase, by incubating a fixed dried cell with a specific probe, which binds to the gene of interest. The gene probe is labeled with fluorescent markers (FISH) and allows numerical chromosome analysis.

7. The advantage of FISH is that, since the cells do not have to be in metaphase, interphase nuclei and even arrested cells can also be analysed. The choice of appropriate probes allow the exact identification of the chromosomes. Unfortunately, only limited numbers of chromosomes can be analysed at one time. However, new developments in the near future eg. Comparative genomic hybridization (CGH), spectral karyotyping (SKY) and DNA chips will allow analysis of all chromosomes.

(ii) Polymerase Chain Reaction

8. Polymerase chain reaction (PCR) allows amplification of well-defined DNA sequences enzymatically in an exponential way. The boundaries of the amplified fragment are determined by a couple of primers which anneal to the denatured template DNA and which then form the starting point of a DNA polymerase to synthesize the complementary strand. The gene of interest is thus amplified for identification.

9. Contamination is an important problem in single-cell PCR : when the sample contains only two copies of the DNA under investigation, one copy of extraneous DNA can lead to misdiaganosis. Two sources of contamination can be distinguished. The first, from cellular sources, contains whole genomic DNA, while the second is carry-over contamination from products of former PCR reactions.

10. Another problem encountered with PCR is allele drop-out (ADO) where an affected allele may fail to amplify during PCR. ADO would create a particular problem for the correct diagnosis of autosomal dominant diseases if the affected allele would fail to amplify and in compound heterozygotes when autosomal recessive diseases were concerned[3].

INDICATIONS

11. Although PGD is an early form of prenatal diagnosis, it will not be an alternative for chorionic villus sampling or amniocentesis in all cases. There are several situations in which PGD would be beneficial:

    (i) In parents who have a genetic diseases or are carriers and have concurrent fertility problems necessitating treatment with IVF
    (ii) Some parents have personal histories of prenatal diagnosis followed by termination of pregnancy for affected fetuses. Some may feel they cannot cope with another failure and would prefer IVF and PGD
    (iii) Another group of patients have moral, emotional or religious objections to termination of pregnancy and see PGD as the only way to have unaffected children

CURRENT STATE OF THE TECHNIQUE

12. Since the first report of clinically applied preimplantation genetic diagnosis[1], the numbers of fertility centers performing PGD and the numbers of PGD treatments have risen steadily.

13. The European Society of Human Reproduction and Embryology (ESHRE) formed a PGD Consortium in 1997 to study the long-term efficacy and clinical outcome of PGD. Their latest published report includes data from 886 couples, 1318 PGD cycles and 162 babies[4]. The data was collected from 27 in-vitro fertilization (IVF) centers who are actively practicing PGD (Table 1). Apart from these centres involved in the Consortium, other centres in the USA, Russia, Belarus, Colombia, Cyprus, Finland, Jordan and Turkey are performing PGD.

14. Apart from aneuploidy diagnosis, several genetic diseases have been tested for. These include autosomal dominant, autosomal recessive and sex-linked disorders (Table II).

15. The data for PGD for aneuploidy screening showed that a total of 6025 oocytes were retrieved, a fertilization rate of 62% was achieved, biopsy was successful in 99% of cases and 63% of embryos undergoing FISH had a diagnosis. Only 36% of embryos were deemed suitable for transfer.

16. The data for PGD of inherited disorders showed that from a total of 10267 oocytes collected, a fertilization of 63% was attained, 81% of embryos were suitable for biopsy and 96% were successfully biopsied. The diagnosis was obtained in 86% of these biopsied embryos and 43% were suitable for transfer. From the initial number of oocytes collected, only 18% were finally diagnosed as suitable for transfer, which confirms the need for the retrieval of large numbers of oocytes for a successful PGD cycle.

PROBLEMS ENCOUNTERED WITH PGD

17. Couples wishing to avail themselves to PGD will have to undergo in-vitro fertilization (IVF). This involves time, expenses and at the end of a cycle, the

uncertainties of success at a pregnancy. It is a process of decreasing numbers as the embryos diagnosed as suitable for transfer will be few.

18. The possibility of a misdiagnosis will be dependent on the experience, care and technical expertise of analysis. Sources of error include mosaicism, contamination of DNA material for PCR and allele drop-out. Hence, most centres still recommend that couples having PGD undergo a confirmation test with prenatal diagnosis.

FUTURE APPLICATIONS OF PGD

19. In future, improved genetic and DNA analysis techniques will improve the accuracy of diagnosis of the preimplantation embryo. There will also be more genes that can be identified and some other applications would include diagnosis of Mendelian disorders using linked polymorphic markers and structural chromosomal abnormalities using centromeric and telomeric probes.

20. As deranged chromosome complements have been identified in first trimester pregnancy failures, aneuploidy screening and transfer of euploid embryos may in future be used to improve assisted reproductive technology (ART) success especially in older patients with repeated IVF failures and recurrent abortions.

21. It is possible that with improved genetic diagnosis, other less fatal or debilitating genetic disorders may be presented as choices for PGD eg. HLA screening, BRCA gene testing for cancer predisposition.

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1. Handyside AH, Kontogianni EH, Hardy K, Winston RML (1990). Pregnancies from biopsied human preimplantation embryos sexed by Y-specific DNA amplification. Nature; 344:768-770.
2. Griffin DK, Handyside AH, Penketh RJA, Winston RML, Delhanty JDA (1991). Fluorescent in-situ hybridization to interphase nuclei of human preimplantation embryos with X and Y chromosome specific probes. Hum Reprod; 6:101-105.
3. Ray P, Winston RML, Handyside AH (1994). Single cell analysis for diagnosis of cystic fibrosis and Lesch-Nyhan syndrome in human embryos before implantation. Miami Bio/Technology European Symposium, advances in Gene Technology : Molecular Biology and Human Genetic Disease; 5:46.
4. ESHRE PGD Consortium Steering Committee (2000). ESHRE Preimplantation Genetic Diagnosis Consortium : data collection II (May 2000). Hum Reprod; 15(12):2673-2683.

TABLE I. Centres Involved in ESHRE PGD Consortium

1	Sydney IVF
2	University of Adelaide
3	Melbourne IVF
4	Centre for Medical Genetics, VUB, Brussels
5	Centre for Preimplantation Genetic Diagnosis, Aarhus University Hospital, Aarhus
6	Hopitaux Beclere et Necker, Paris
7	Institut de Genetique et de Biologie Moleculaire et Cellulaire, Strasbourg
8	St Sophia's Childrens Hospital, University of Athens
9	IVF and Genetics, Athens
10	Department of O&G, Rambam Medical Centre, Haifa
11	IVF and Infertility Centre, University of Bologna
12	SISMER, Bologna
13	PGD Working Group, Maastricht
14	Stichting Klinische Genetica Zuid-Oost Nederland, Maastricht
15	Department of O&G, Samsung Cheil Hospital, Sungkyankwan University, Seoul
16	Instituto Dexeus, Barcelona
17	Unitat de Biologia Cellular, Univ. Autonoma, Barcelona
18	Department of Clinical Genetics, Karolinska Hospital, Stockholm
19	Assisted Conception Unit, St. Thomas' Hospital, London
20	Department of O&G, University College, London
21	Institute of O&G, RPMS, Hammersmith Hospital, London
22	School of Biology, University of Leeds, Leeds
23	Department of O&G, Baylor College of Medicine, Houston, Texas
24	Department of O&G, University of Florida, Florida
25	Jones Institute for Reproductive Medicine, Norfolk, Virginia
26	New York University Medical Center, New York
27	Institute of Reproductive Medicine and Science, St Barnabas Medical Center, New Jersey

TABLE II. Genetic diseases that have been tested with PGD

• Autosomal recessive	• Cystic fibrosis • Beta-thalassaemia • Spinal muscular atrophy • Tay-Sachs disease • Rh Isoimmunization • Gaucher disease • Sickle cell anaemia
• Autosomal dominant	• Myotonic dystrophy • Huntington's disease • Charcot-Marie-Tooth disease • Neurofibromatosis type I • Marfan syndrome • Osteogenesis imperfecta
• Sex-linked	• Duchenne and Becker's muscular dystrophy • Haemophilia • Fragile-X syndrome • Mental retardation • Wiskott-Aldrich syndrome • Charcot-Marie-Tooth • Retinitis pigmentosa

LEGAL AND ETHICAL ISSUES PERTAINING TO PREIMPLANTATION GENETIC DIAGNOSIS

Introduction

1. Preimplantation Genetic Diagnosis (PGD) is a procedure that aims to select genetically defective embryos before they have a chance to develop. It is a procedure that is done in conjunction with in vitro fertilization (IVF). Hence it is necessary to outline the legal and ethical implications of IVF as they are relevant to the discussion of the issues related to PGD.

Relevant Legal Issues

(1) Eligibility/Access to Treatment

2. Currently, there is no specific legislation relating to the entitlement of a person to gain access to treatment services. In the Singapore context, due to the social and economic mores of our society, this treatment (if approved) will be restricted to only married heterosexual couples who may or may not be fertile.

3. However in the absence of any legislation or case law supporting this situation, potential problems may arise in the event a determined couple who does not fit into this category wants to have this procedure performed. There is nothing to stop them from trying to enforce their desire in court.

4. But given the prevailing situation in Singapore which is generally a non-litigious society and where such unconventionality is frowned upon, it is an unlikely scenario. However in order to avoid this problem, it is necessary to list down clearly the prerequisites that must be fulfilled in order to be eligible and have access to treatment and draw up a list of guidelines to make sure they are strictly enforced to avoid any ambiguity.

(2) Conscientious Objection

5. The right to 'conscientious objection' is contained in section 6 of the Termination of Pregnancy Act (Cap 324). Section 6 provides as follows:

6. (1) Subject to subsection (3), no person shall be under any duty whether by contract or by any statutory or legal requirement to participate in any treatment to terminate pregnancy authorised by this Act to which he has a conscientious objection.

(2) In any legal proceedings the burden of proof of conscientious objection referred to in subsection (1) shall rest on the person claiming to rely on it and that burden may be discharged by such person testifying on oath or affirmation that he has a conscientious objection to participating in any treatment to terminate pregnancy.

Although it is a provision that relates to the termination of pregnancy, it may be invoked in an analogous situation such as the performing of a PGD or IVF procedure. Essentially, the right to conscientious objection allows a doctor, nurse or other individual to refuse to 'participate' in a licensed activity to which they have such a conscientious objection. Such a matter of conscience is widely understood to cover religious, moral or other principled beliefs that lead the individual to conclude that the activity is wrong.[1]

7. In trying to establish when such a right may be used, difficulties may arise. It is not clear whether the individual must object to participating in a whole class of activity or whether he may also object to participating only in particular situations or parts of a licensed activity.

8. An example cited by Ian Kennedy and Andrew Grubb of how such a right may be exercised is as follows. Would an individual's objection to being involved in embryo biopsy fall within such a right even if he has no objection to IVF in principle? There is no clear answer though they are of the view that it may be argued that this right only permits an individual to have a conscientious objection to a class of activity but does not allow an individual to pick and choose which parts of the licensed activities he is prepared to be involved in.[2]

(3) Consent to Use and Control of Genetic Material

9. Consent is relevant in two distinct ways. First, there is a need for those who are donating genetic material and those being treated for infertility to consent to the medical procedure. Secondly, the issue of consent arises with regard to the future use or storage of an individual's genetic material.

(a) Consent to the Procedure

10. A donor of genetic material or a patient undergoing infertility treatment must consent to the medical interventions involved. This is to avoid any later difficulties that may arise in trying to establish the legitimacy of the child born after treatment.

11. In Singapore, the Law Reform Committee of the Singapore Academy of Law produced a report on the status of children born through artificial conception in 1995. A bill entitled the Status of Children Act has been proposed so as to clear up the issue of the legitimacy of a child conceived in such a manner. Though not yet enacted into law, it would be useful to refer to it. The URL is as follows:

http://www.lawnet.com.sg/freeaccess/lrcr/Artificial_Conception.PDF

(b) Control of gametes and embryos

12. The issue at hand here concerns the extent to which the providers of gametes and embryos may exercise legal control over their genetic material. Currently there is no legislation or cases in Singapore which address the issue in question.

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[1] Ian Kennedy, Andrew Grubb, *Medical Law: Text with Materials*, 2nd ed Butterworths, London (1994)
[2] *Ibid*

What may be helpful here is the position in England under the Human Fertilization and Embryology Act 1990 (Cap. 37 of 1990) ("the HFEA"). There is an elaborate scheme of consents that vests control of gametes and embryos in the providers of the genetic material. Schedule 3 to the Act requires that a gamete provider must, at the time that the gametes are procured, indicate in a written consent what use(s) those gametes may be put to. The gametes (or any resulting embryos) may only be used in accordance with those consents.

13. It is recommended that a regime that will specifically address this issue as to who has control over such genetic material be established. It will be prudent to state clearly who possesses such control and how excess genetic material will be treated (destroyed, used for further research, etc). It is emphasized that this issue of consent with respect to control is a very important issue that needs to be clarified before anything medical procedure begins.

14. The current state of the law is not clear. However there is a great potential that a Pandora's box may be opened if such a regime is not properly established before treatment begins. Issues such as whether these embryos are to be considered as human or not and who has the right to decide the fate of the genetic material are examples of the thorny issues that may arise if this issue is not properly addressed prior to the beginning of treatment.

15. It will be useful to see how the US attempts to address this issue. The American Bar association has come up with a discussion draft entitled 'Model Assisted Reproductive Technologies Act' which may be view online at

http://www.abanet.org/ftp/pub/family/art_monograph.doc

(4) Medical Confidentiality

16. Every doctor has a duty of confidentiality to his patients, a duty founded in the medical codes of ethics and the law. The basis of the common law duty of confidence is for the benefit and protection of the patient. Hence it is not absolute and may be waived or released by the patient.

17. In the context of PGD, it follows therefore that a doctor is not to disclose to the parties involved each of the other's medical information in the absence of the parties' consent. A breach of patient confidentiality renders a doctor liable to disciplinary action by the profession as well as legal liability with respect to the patient. A patient may file a negligence suit in the event any unauthorised disclosure of confidential information causes him damage.[3]

18. In order to avoid legal liability, a doctor must obtain a patient's consent to communicate information about his medical condition. Such consent may be obtained expressly or impliedly. Disclosure should only be done in appropriate circumstances and patients should be told when such information is to be disseminated.

[3] Catherine Tay, *Medical Confidentiality: Ethical & Legal Issues*

(5) Negligence

19. As a tort, negligence consists of a legal duty to take care and breach of that duty by the defendant causing damage to the plaintiff.[4] With respect to medical law, there are two aspects of medical negligence that are of relevance here namely negligent counseling and negligent diagnosis.

(a) Counseling and Negligence

20. One of the most significant issues in recent years is the amount of information which a patient ought to be given if a doctor is acting with due professional skill and care. If the doctor fails to give the patient the amount of information which ought to be given, it is now generally held to amount to negligence in law.[5]

21. If a genetic counselor or doctor fails to advise prospective parents of the risk (however small) of genetic illness in the foetus, the parents of an afflicted child may choose to raise an action against him in respect of his negligence. In the United Kingdom, there is no doubt that damages will be awarded in respect of negligent counseling.[6]

22. The concept of informed consent whereby a doctor is under a fiduciary duty to ensure that a patient understands what the risks are involved in undergoing or foregoing certain treatment forms part of the law in the US and Canada. Singapore however does not ascribe to that practice as we follow the English position which provides that so long as the doctor follows the practice adopted by a responsible body of doctors in relation of what or what not to tell, he or she will not be negligent.

(b) Diagnosis and Negligence

23. The *Bolam* test is the controlling test in Singapore with respect to medical negligence. It is stated as follows:

> "The test is the standard of the ordinary skilled man exercising and professing to have that special skill. A man need not possess the highest expert skill at the risk of being found negligent ... it is sufficient if he exercises the ordinary skill of an ordinary competent man exercising that particular art."

24. In essence, a doctor will not be found negligent if he exercises reasonable care and skill. Even if there is a body of opinion that takes a contrary view, a doctor is not negligent if he is acting in accordance with such a practice. Thus liability only arises if a doctor fails to match that standard of care in carrying out his duty as a professional.

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[4] Michael A. Jones, *Textbook on Torts,* 5th ed Blackstone Press Ltd, London (1997)
[5] Douglas Cusine, *Legal issues in human reproduction,* Dartmouth Publishing Co Ltd, England (1989)
[6] Mason & McCall Smith, *Law and Medical Ethics*, 4th ed Buttterworths, London (1994)

Relevant Ethical Issues

25. Artificial reproductive techniques raise difficult ethical issues. Objections to such procedures include the argument that they should not be acceptable because they are 'unnatural'. Such techniques are deemed 'unnatural' in the sense that the 'sacred process' of life is the prerogative of God and should not be interfered with.[7] This argument promotes the view that procreation should only be done in the way God intended which is through sexual intercourse. However as argued by Athena Liu, this line of argument is vague and is clearly not a belief rigidly adhered to by those who are prepared to used artificial techniques to procreate and thus should not seriously suggest that these people's view should be converted.

26. A second interpretation of the 'unnatural' argument is based on the belief that these techniques contravene the 'natural law'. The objection here is that such reproductive techniques sever the link between the natural and legitimate end of sex and are thus contrary to natural law. This view however fails to establish what useful purpose it seeks to uphold and should not pose a serious threat to such artificial reproductive techniques.

27. Yet another objection to such procedures is the fear of potential abuse that will lead to the development of a eugenics program. Using PGD to avoid transmitting a genetic predisposition or a characteristic trait that is deemed undesirable or to choose the sex to select the desired qualities of the unborn child is unacceptable.[8] Hence it is recommended that PGD be strictly used only in situations where the goal is to prevent the transmission of a serious genetic disease. Guidelines should be drawn up and strictly adhered to so as to quell such fears that eugenics practices may emerge.

28. Another significant ethical issue is with respect to embryos that are not implanted. There are religious and ethical objections to such embryos being used for research and experiment purposes. These views are founded on the basis that such practices are tantamount to meddling with the sanctity of life. However, proponents of experimentation argue that embryonic research is necessary for human welfare for the development and refinement of present procedures as well as to lead to a greater understanding of early embryonic development, survival and implantation and its subsequent evolution.[9]

Conclusion

29. As outlined above, the legal issues pertaining to PGD should be viewed in conjunction with those of IVF as they are inextricably linked. It would be wise if a doctor is cognizant of all the possible pitfalls and take all the necessary precautions to avoid them.

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[7] Athena Liu, *Artificial Reproduction and Reproductive Rights*, Dartmouth Publishing Co Ltd, England (1991)
[8] Supra n. 1
[9] Supra n. 7

30. As for the ethical issues, there will always be fears and objections against procedures of this nature. Sometimes the opposition may be vociferous in their objection. However, so long as there are strict guidelines in place to ensure that doctors do not attempt to 'play God' and that the sanctity of life is given its due respect, such procedures should be given the go ahead for the betterment of Mankind.

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Singapore General Hospital

Ms Laura Liew
National University of Singapore

ANNEX F

BIOETHICS ADVISORY COMMITTEE (BAC)
HUMAN STEM CELL RESEARCH CONSULTATION PAPER (8 Nov 2001)
DISTRIBUTION LIST

#	Name	Designation	Organisation
1	Prof Feng Pao Hsii	Chairman	National Arthritis Foundation
2	Dr Tan Kok Hian Kelvin	President	Obstetrical & Gynaecological Society of Singapore
3	Ms Winnie Tang	President	Singapore National Stroke Association
4	Dr Lewis Lee	President	Singapore Dental Association
5	Dr Warren Lee	Chairman	Diabetic Society of Singapore
6	Dr Low Lip Ping	Chairman	Singapore National Heart Association
7	Dr Mary Ann Tsao	President	Tsao Foundation Ltd
8	Mr Tan Geok Tian	Chairman	Singapore Cancer Society
9	Dr Tan Hiang Khoon	Chairman	Children's Cancer Foundation
10	Mr Gerard Ee	Chairman	Singapore Hospice Council
11	Dr Daphne Khoo	President	Endocrine and Metabolic Society of Singapore
12	Mr Harbans Singh PS	Secretary	Inter-Religious Organisation, Singapore
13	Mr V R Nathan	Chairman	Hindu Endowments Board
14	HJ Maarof Salleh	President	Majlis Ugama Islam Singapura (MUIS) (Islamic Religious Council of Singapore)
15	Bishop John Tan	President	National Council of Churches of Singapore
16	Mr Bhajan Singh	Chairman	Sikh Advisory Board
17	Venerable Shi Ming Yi	Secretary General	Singapore Buddhist Federation
18	President	President	Singapore Chinese Buddhist Association
19	Dr Lee Soon Tai	President	Singapore Council of Christian Churches
20	President	President	Taoist Federation (Singapore)
21	Dr Hui Keem Peng John	Master	The Catholic Medical Guild of Singapore
22	President	President	The Jewish Welfare Board
23	Bishop Dr Robert Solomon	Bishop	The Methodist Church in Singapore
24	The Honourable Justice L P Thean	Chairman	Law Reform Committee, Singapore Academy of Law
25	Mr Palakrishnan, SC	President	The Law Society of Singapore
26	Dr Walter Tan	Master	Academy of Medicine, Singapore
27	A/Prof Cheong Pak Yean	President	College of Family Physicians, Singapore
28	Prof Low Cheng Hock	President	Singapore Medical Association
29	Dr Lee Suan Yew	President	Singapore Medical Council
30	Ms Susie Kong	President	Singapore Nurses Association
31	Ms Ang Beng Choo	Registrar	Singapore Nursing Board
32	Prof Chew Yong Tian	President	Biomedical Engineering Society (Singapore)
33	Dr Sara Zaman	Secretary	Singapore Society for Microbiology & Biotechnology
34	Dr Eric Yap	President	Biomedical Research & Experimental Therapeutics Society of Singapore
35	Dr Koh Lip Lin	President	Singapore Association for the Advancement of Science
36	A/Prof Shirley Lim Siew Lee	President	Singapore Institute of Biology
37	Prof Leo Tan Wee Hin	President	Singapore National Academy of Science
38	Mrs Catherine Seah	Chairperson	Science Teachers Association of Singapore
39	Dr Khoo Hoon Eng	President	Singapore Society for Biochemistry & Molecular Biology

ANNEX G

WRITTEN SUBMISSIONS TO HUMAN STEM CELL RESEARCH (HSR) CONSULTATION PAPER

A. MEDICAL AND HEALTH ORGANISATIONS

1. National Arthritis Foundation
2. Singapore Dental Association
3. Obstetrical and Gynaecological Society of Singapore

B. RELIGIOUS GROUPS/ORGANISATIONS

The Inter-Religious Organisation of Singapore ('IRO') obtained views from the Hindus, Taoists, Roman Catholics, Sikhs, Bahai faith, Jewish faith:

1. Hindu Endowments Board *(submitted under the IRO)*
2. Taoist Mission (Singapore) *(submitted under the IRO)*
3. St. Anthony's Canossian Convent *(submitted under the IRO)*
4. Sikh Faith view *(submitted under the IRO)*
5. The Spiritual Assembly of the Baha'is of Singapore Ltd *(submitted under the IRO)*
6. The Jewish Welfare Board *(submitted under the IRO)*
7. Singapore Buddhist Federation
8. The Catholic Medical Guild of Singapore
9. National Council of Churches of Singapore
10. Singapore Council of Christian Churches
11. Majlis Ugama Islam Singapura

C. PROFESSIONAL GROUPS

1. Law Reform Committee, Singapore Academy of Law
2. The Law Society of Singapore
3. Singapore Hospice Council
4. Singapore Medical Association
5. Singapore Medical Council
6. Singapore Nurses Association
7. Singapore Nursing Board

D. SCIENTIST/RESEARCHER GROUPS

1. Biomedical Engineering Society (Singapore)
2. Science Teachers Association of Singapore
3. Singapore National Academy of Science
4. Singapore Society for Biochemical and Molecular Biology

E. OTHER

Personal View from an IRO member *(submitted with the IRO response)*

A. MEDICAL AND HEALTH ORGANISATIONS

1. National Arthritis Foundation
2. Singapore Dental Association
3. Obstetrical and Gynaecological Society of Singapore

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Dr Wee Kim Wee
Patron

19 December 2001

Professor Lim Pin
Chairman
Bioethics Advisory Committee
250 North Bridge Road
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Singapore 179101

Dear Prof Lim Pin

REQUEST FOR FEEDBACK REGARDING HUMAN STEM CELL RESEARCH IN SINGAPORE

I refer to your letter dated 8 November 2001 regarding the above.

The National Arthritis Foundation thanks you and your Committee for asking our views. This matter was tabled at our regular Executive Committee meeting on 13 December 2001.

The members concur very much with the views of the Bioethics Advisory Committee as laid out in your statement. We are mindful of the great potential of Stem Cell Research in terms of therapy of certain diseases but at the same time, controls and guidelines need to be in place.

The Foundation will support in full any measures the Bioethics Advisory Committee feel necessary in the context of Singapore's religious, patient, medical and scientific organisations and groups.

With best regards

Yours sincerely

Prof Feng Pao Hsii
Chairman
National Arthritis Foundation

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SINGAPORE DENTAL ASSOCIATION

15th December 2001

Bioethics Advisory Committee
250 North Bridge Road
#15-01/02 Raffles City Tower
Singapore 179101
Attn: BAC Secretariat

Dear Prof. Lim

Re: Feedback on Human Stem Cell Research in Singapore

There are numerous issues involved in embryonic stem cell research. Aside from the push from some scientific communities towards less impediment in research on embryonic stem cells, and our government is also pushing for developing biotechnology as a cornerstone of our future economy. We need to struck a suitable balance between ethics and relentless pursuit of science.

An embryo has all the innate potential to be a viable being. Many questions and issues must be answered before attempts to conduct any experiments on any embryo.

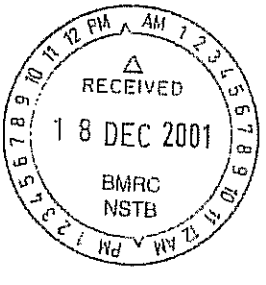
1) It is preferable for us to avoid having to work on embryos for the purpose of obtaining stem cells.

2) Although it is proven to be more difficult, emphasis or added effort should be applied to explore other methods to source for stem cells.

3) If a decision is made to use embryos as a source of stem cells then air-tight controls must be in place to ensure an absolutely transparent and acceptable protocol in sourcing for suitable embryos.

Yours faithfully,

Dr Chung Kong Mun
Singapore Dental Association
Committee Member



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30 November 2001

Prof Lim Pin
Chairman
Bioethics Advisory Committee
250 North Bridge Road #15-01/02
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Singapore 179101

Dear Prof Lim,

Request for Feedback regarding Human Stem Cell Research in Singapore

Thank you for your letter dated 8 November 2001, inviting our society (The Obstetrical & Gynaecological Society of Singapore - OGSS) to give our feedback.

Within the short span of time given, our society has circulated the BAC paper among our over 300 members to invite written comments and has conducted a meeting for members to air their views.

With regards to the positions on research of adult stem (AS) cells and on reproductive cloning, the views of those who expressed themselves in written comments or in the meeting thus far, are in general agreement with BAC. We are generally thus far, for research of adult stem cells but are not in favour of reproductive cloning.

However with regards to the views on research of embryonic germ (EG) cells, on research on early embryos < 14 days old and on therapeutic cloning, the members of our society have differing (for, neutral or against) views, reflecting the diversity of opinions among our members. This would not be surprising, considering that our members, though professionals (mainly obstetricians/gynaecologists as well as obstetricians/gynaecologists in training, scientists and doctors) have differing backgrounds in terms of age, sex, race and religion. Our members also have differing views on abortion. A number of our members have conscientious objection to participate in treatment to terminate pregnancy under the Termination of Pregnancy Act, Singapore. We are therefore unlikely or rather it is impossible to forge a consensus opinion

on these 3 issues among our members, especially when developments within these issues are also rapidly evolving in the whole world.

It is timely that the BAC is looking closely at issues involving stem cell research in Singapore. We feel that there would be a constant need to review recommendations, policies and regulations in human stem cell research, in view of the very rapid developments in this area, around the world.

We will compile and send you the comments from individual OGSS members or groups of OGSS members once we have the consent from them within 2 weeks.

Yours sincerely

Dr Tan Kok Hian, Kelvin
President

ogss/letter/149

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15 December 2001

Prof Lim Pin
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Dear Prof Lim Pin

Human Stem Cell Research in Singapore Feedback - follow-up letter

Thank you for your letter of 4 December 2001. As mentioned in our letter of 30 November 2001, we are attaching the views of the 5 OGSS members who gave written submission.

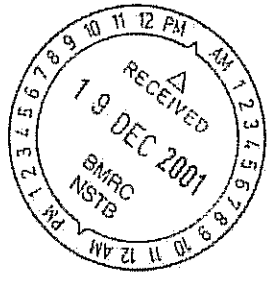
We are also attaching the results of a simple survey (including the survey form), which was sent to 300 of our members on 5 December 2001 for them to air their views. A total of 56 OGSS members responded within a week and the results of these early respondents were compiled.

We would not be requesting for a dialogue session but would be pleased to answer further queries you may have.

Thank you and warm regards. Merry Christmas!

Yours Sincerely,

Dr Tan Kok Hian Kelvin
President



Reply to the BAC Position Paper on Stem Cell Research

The progress in stem cell research has brought with it new hopes in the treatment of diseases, tissue regeneration and engineering. This will bring about significant changes in the management of clinical diseases. Should this form of therapy become a reality, national security should be considered and Singapore should not fall behind in this biotechnology frontier. Since we already have a head start with the development of embryonic stem cell lines, it would be imperative to develop research in differentiation of these stem cell lines for therapy and we appreciate the BAC's stand allowing research using embryos up to 14 days for this purpose. This is similarly approved in the United Kingdom.

The use of fetal germ cell lines for the production of stem cells should come under strict regulations that also apply to fetal tissue transplantation. Consent for termination of pregnancy should be independent of the creation of stem cell lines. Thus, it would be imperative that cadaveric fetal tissue and embryos should not be bought or sold for research purposes.

We certainly support the concerns of the BAC with regard to reproductive cloning and agree that this should not be allowed in Singapore. However, it is indeed an enlightened opinion to allow the use of therapeutic cloning to produce embryos from nuclear transfer for production of stem cells. As there can be a potential move from therapeutic to reproductive cloning, we feel that the ethical approval for such research work should come under a common body (eg. BAC) which would also facilitate close monitoring of such activity and the enforcement of guidelines. If the ethical approval for research work involving nuclear transfer and stem cell production is decentralised to the various funding bodies, active monitoring and policing may not be as efficient.

Prospective donors of embryos for stem cell research should receive timely, relevant and appropriate information to make informed and voluntary choices regarding the disposition of their embryos. They should also be given the equal options of storing the embryos for their own future use, donating them to other women or discarding them. Information sheets and appropriate consent forms could be drafted by the BAC for common use in the various assisted reproduction centres in Singapore.

We feel that the need for national oversight and review of human stem cell research is crucial. This body would serve to constantly review the ethical and legal issues and ensure strict adherence to guidelines and standards in the country. A registry of approved research projects, facilities and established stem cell lines should be kept and monitored.

It is indeed timely that the BAC has been set up to look closely at issues involving stem cell research. We applaude the painstaking efforts that the BAC has taken in culling a variety of opinions on this issue. With your guidelines, we hope that stem cell research in Singapore can be taken to new heights.

Dr Christine Yap
OGSS Member 22 Nov 2001

Founded 1905

THE NATIONAL UNIVERSITY *of* SINGAPORE

Department of
Obstetrics & Gynaecology

22 November 2001

Dr Tay Eng Hseon,
Honorary Secretary,
OGSS,
C/o KK Women's & Children's Hospital,
Unit 8K38 (Level 8), Women's Tower,
Singapore 229899

Fax: 65-229-1969

Dear Eng Hseon,

FEEDBACK: HUMAN STEM CELL RESEARCH IN SINGAPORE

I write in response to your letter of 16 Nov 2001 regarding the BAC's paper on the above.

It is a measured and balanced opinion on this very fast-expanding field. I support the conclusions made in the document. I must also state that I was in the sub-committee that prepared the background paper for the BAC, though I was not in the Committee that proposed the final draft.

To prevent abuse (especially to prevent human reproductive cloning) I support the need for a watch-dog body with adequate disciplinary powers. How this is formed and the composition of this body needs to be carefully thought-out. Reproductive cloning should be allowed for other species, especially in wildlife conservation, agricultural animals and animals of high value (eg pets, and race-horses).

Therapeutic cloning has tremendous potentials, and should be allowed. It is likely that it will blossom into a new life-science industry for Singapore. Hence, allowing it will be beneficial to Singapore's survival in a highly competitive world. Ethically, there is still an intermediate stage where embryos are created. But just as unwanted extra human embryos from IVF programs are allowed to be used for the generation of embryonic stem cells, they should be allowed to develop stem cells that are genetically from the donor, to be used by the donor ("autologous" use).

Yours Sincerely,

Ng Soon Chye, MD, FRCOG,
Professor.

FACULTY OF MEDICINE • NATIONAL UNIVERSITY HOSPITAL • LOWER KENT RIDGE ROAD • SINGAPORE 119074
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KK WOMEN'S
AND CHILDREN'S
HOSPITAL

22 November 2001

Dr Kelvin Tan
President O&G Society
Singapore

Dear Dr Kelvin Tan

RE: FEEDBACK ON PAPER ON HUMAN STEM CELL RESEARCH

Thank you for asking our feedback.

1. Personal

I am of the opinion that the paper that has been prepared has been carefully done. They contain current views of world experts in the field concerning the matter. Also, I was happy to note the conservative stance of the committee. This reflects our Singaporean multi-ethnic and multi-religious society with our own convictions on ethical standards.

I would not agree on obtaining stem cells from embryos, but would not oppose others who would. I would agree with a suggestion in the Forum page that we should research more into umbilical cord stem cells; also adult stem cells. The processes to encourage proliferation and usefulness of the latter two types of stem cells have yet to be exhausted.

With our existing system of reporting on IVF and other ART procedures, it should not be difficult to incorporate details of reporting stem cell research and its outcome to the central repository. This would provide for public accountability.

2. OGSS stance

Although time is short, it would be good to have a debate on paper by interested members from the Society, especially from the O&G departments from NUH, SGH and KKH. We could also ask Prof Arif Bongso to speak of his experience and discovery. Following this we could then collate personal replies as well as conclusions arising from the debate. We would then have an OGSS stand on human stem cell research.

Best wishes,

Yours sincerely,

Dr Lawrence Chan

100
BUKIT TIMAH
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VIEWS ON HUMAN STEM CELL RESEARCH

Embryonic stem cell (hES) lines derived from the inner cell mass of blastocysts holds promise of tremendous benefits to mankind.

SCIENTIFIC VIEW: From the scientific point of view, I would encourage research on hES cells because research on ES cells would lead to the cure of many diseases human beings suffer from. Research should be carried out using the existing stem cell lines. Since the existing lines are derived using mouse feeder layers, there is concern about virus and genetic contamination of ES cells. Whether the final product derived from such cell lines can be used for human transplant (Xenograft) should be addressed clearly. This is not allowed in the USA.
If the existing stem cell lines cannot be used due to the above reason or due to other reasons such as immuno-rejection, which necessitates the use of more embryos to produce new stem cell lines, then strict monitoring is required. Institutes, particularly fertility centres should seek the permission of BAC after obtaining consent from the patient who donates embryos for such purpose and necessary documents must be in place.

ETHICAL VIEW: Human oocytes after fertilization form zygotes, which in turn form embryos and blastocysts on day 5 or 6 after which the inner cell mass are used to derive the ES cells. From the time of fertilization, zygotes are considered as a living being. It deserves moral attention and is considered as having the potential to become a human being. However the neural tube develops after 14 days of its life, it doesn't feel the pain until then. In Singapore, according to the guidelines to practice IVF, research can be carried out on embryos until 14 days and similar guidelines should be place for ES cell research with strict monitoring on the use additional embryos for research. My views are not in favour of any kind of research on human cloning.

Dr. Christopher Chen
O & G Society Member

23 Nov 2001

Douglas Ong Clinic for Women – Fetal Medicine and Urogynaecology
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Telephone: (65) 762 8066 or 894 7516 Email: MyGynae@Douglas-Ong.com

Fax Cover Form (Medical Data) – Medical In Confidence

To: Dr Kelvin Tan / Tay EH
O&G Society

Fax: 299 1969
Date / Time: 29 Nov 2001

Number of Pages (including this page) – 7

MESSAGE: STEM CELL RESEARCH FEEDBACK

Dear Kelvin / Hoon .

Thanks for taking the time to read this.

I would greatly appreciate your support on this feedback. As you know the Bioethics Advisory Committee has asked for feedback on stem cell research. They have also asked the O&G Society for feedback. I intend to send this letter to both OGSS as well as direct to BAC.

The essence of this paper is that it :

a) Approves and supports adult stem (AS) cell research
b) Is neutral about embryonic germ (EG) cell research
c) Is against embryonic stem (ES) cell research
d) Endorses Bioethics Advisory Committee stand against all forms of reproductive cloning
e) Is against any form of therapeutic cloning
f) Requests government oversight on stem cell research
g) Requests information to be open to public scrutiny
h) Endorses the right of the embryo as a human being regardless of stage of development

I would appreciate your help in the following ways:

a) If you are an OBGYN, to allow me to append your name and MCR to the letters to OGSS and to BAC
b) If you are non OBGYN to allow me to append your name and MCR to the letter to BAC.

Grateful for your support. My personal thanks.

Doug

IMPORTANT - Please call us if you have received an incomplete fax :

28 November 2001

Dr Tay Eng Hseon
Honorary Secretary
Obstetrical & Gynaecological Society of Singapore
C/o KK Womens and Childrens Hospital
Unit 8K38 Womens Tower
100 Bukit Timah Road
S'pore 229899

Dear Dr Tay,

Human Stem Cell Research in Singapore - Feedback

Thank you for your letter inviting feedback from members on this subject.

The subject of stem cell research and human cloning is without doubt one of the most divisive and contentious issues to face our generation. We are profoundly aware of the diverse and strongly held views and would like to share our personal insights.

With specific reference to the consultation paper issued by the Bioethics Advisory Committee (BAC), we have the following points to raise:

1) We recognize that genuine steps have been taken by the government to assure appropriate dialogue and feedback. In particular we welcome the establishment of a watchdog body with no conflicting interest in the development of stem cell research. We appreciate their work and time invested thus far.

Ethical and Social considerations:

2) We welcome the BACs view of "the special status of an embryo as a human being". While we should support research that can ameliorate and ultimately cure disease, we need to start from the premise that those who are seen to hold the key to these problems are fellow human beings with inherent worth.

3) However, BAC takes the view "that it is justified to use early embryos, not more than 14 days old" based on the principle that "human embryos which are less than 14 days old have no pain or sentience".

    a) This view, propagated in the UK Warburg Report of the late 1970s was even at that time held to be controversial and was seriously challenged. Despite objections, it was used as the basis for the UK Human Fertilisation and Embryology Act 1990. Nonetheless it has been since been accorded the dignity of time. In light of scientific advances, it would be appropriate to re-examine, challenge and debate this relatively old piece of research which many countries have since adopted as fact.

    b) The use of pain as a means of differentiating the value of life is fallacious and worthy of condemnation. Taken *in extremis*, persons born with congenital absence

Further, absence of pain does not mean absence of life. Plants are undoubtedly alive. Gametes are undoubtedly alive. In the same vein, embryos less than 14 days old are undoubtedly alive.

c) We hold the view that life is a continuum.

In 1994, the chief scientist advising the NIH Human Embryo Research Panel on modern embryology testified "that human development is a continuum from the moment when the nuclei of sperm and egg combine in the new embryo".

4) Rights of the embryo – BAC has drawn its position widely from many countries "including the UK, USA, Australia, New Zealand, Israel and Japan". In particular, embryo protection is addressed in extensive reference to the Human Fertilisation and Embryology Authority (HFEA) in the UK.

a) While authoratitive in its derivation, the list is not exhaustive. We would like to draw BAC's attention to other position papers:

i) UNESCO's *Universal Declaration on the Human Genome and the Protection of Human Rights* maintains that: "no research applications should be allowed to prevail over the respect for human dignity and human rights, in particular in the fields of biology and genetics."

A universal declaration, when adopted, is an international statement of principles that eventually may become part of customary law and so have force of law, but *ab initio* serves a hortatory function and is meant to guide nations in their domestic legislation.

ii) Council of Europe –

In 1996, the Council of Europe (40 countries) *Convention on Human Rights and Biomedicine* stated "Parties to this Convention shall protect the dignity and identity of all human beings and guarantee everyone, without discrimination, respect for their integrity and other rights and fundamental freedoms with regard to the application of biology and medicine."[1]

In 1990, the Council also stated in its preamble to *Medical Research on Human Beings* that "medical research should never be carried out contrary to human dignity."[2]

In 1989 the Council, in their *Recommendation on the Use of Human Embryos and Fetuses in Scientific Research* provided that "the removal of *cells*, tissues, or embryonic or fetal organs, or of the placenta or the membranes, if live, for investigations other than of a diagnostic character and for preventive or therapeutic purposes shall be prohibited"[3]. This last statement is relevant as it addresses the issue of removal of cells from human embryos

At the international level, then, there is no doubt that respect for human dignity and respect for the intangibility of the human body, its constituent parts, reproductive tissues, and even down to the cell(s) are irreparably linked.

b) The BAC correctly points out that "disagreements arise regarding ... what form such respect (of human life) should take and what level of protection is required". These references make a clear stand from broad based groupings such as the UN and Council of Europe - as opposed to views from individual countries.

c) We note that no reference has been made to any of the countries where embryo research is banned or severely restricted. Four countries prohibit experimentation with fertilized eggs (Norway) or with human embryos (France), or experiments which have as their purpose "developing methods for achieving potentially hereditary genetic effects" (Sweden), that is, to "develop certain characteristics" (Switzerland). Such policies should also be examined to provide some balance to BAC's work.

d) We hold the view that the embryo deserves the full protection of society because of its moral status as a person. There is no such thing as a "potential human being" inasmuch as one cannot be "slightly pregnant".

Research on AS (Adult Stem) cells

5) We agree completely with BAC's stand that there should be no ethical objections to AS cell research.

Research on EG (Embryonic Germ) cells

6) BAC correctly states that "there are no new ethical issues arising from the use of such cells so long as the decision taken to abort is taken separately and independently from the decision and consent to extract EG cells".

We do not condone abortion. However, for persons who choose to abort their child, in this respect we are in agreement. We hope that requirements for donation of cadaveric fetal tissue for research should be clearly spelt out. In particular, these should address the issues of:

a) Assurances that there are no inappropriate incentives in the decision to abort.
b) Assurances that there are no direct therapeutic incentives to create or abort.
c) Prohibition of monetary incentives or purchase, sale or directed donation of such tissue for commercial purposes.

Research on ES (Embryonic Stem) cells

7) Our view of research on embryos less than 14 days old has been addressed earlier. We are opposed to all forms of ES research on ethical and moral grounds.

8) However if BAC holds to its position as outlined in its consultation paper, then we hope for the following issues to be addressed:

a) Detailed legislation on
    i. the derivation and

ii. use of ES cells

b) ES cells are to be derived solely from excess embryos intending to be discarded after IVF for infertility treatment.
c) Legislation should be provided against direct therapeutic incentives to create or abort such embryos.
d) Legislation should be provided against monetary incentives or purchase, sale or directed donation of such embryos for commercial purposes.

Research on Human Reproductive Cloning

9) We strongly support BAC's stand against reproductive cloning. We are similarly opposed to the Kantian view of the utility of human life as a means to an end.

10) In its paper, BAC appears to restrict its overview of cloning to cell nuclear transfer. We wish to point out that presently, cloning may also arise from a technique called nuclear splitting and hope that this and other future techniques will be addressed by the BAC.

11) We note that there may be deficiencies in explicit legislation of definitions in a rapidly developing science. Perhaps a blanket cover would be preferable to narrow definitions which may be outdated faster than legislation can change.

Research on Human Therapeutic Cloning

12) The BAC has left open the issue of human therapeutic cloning noting that "it appears to be an essential part of human stem cell research" and is prepared to support its use under strict supervision.

13) We disagree with this stand for the same reasons as we disagree with ES research. We hold that all forms of human cloning be banned. We put it to the BAC that a more coherent policy may be achieved through an outright ban on all forms of cloning, therapeutic or reproductive.

14) Should BAC maintain its recommendation, we wish to see that initiation of therapeutic cloning (if and when it occurs) should be subject to the same review and open dialogue as has occurred with human stem cell research – and not as BAC currently recommends "on a case to case basis with proper consent and under appropriate governmental oversight". Such decisions should be subject to open feedback and not left in the hands of a few.

In an ethically sensitive area of emerging biomedical research it is important that all members of the research community, whether in the public or private sectors, conduct their research in a manner that is open to appropriate public scrutiny.

Government oversight

15) We welcome the BACs recommendation for "a well established and effective framework for the control of research involving embryos in Singapore".

16) We hope to see the establishment of a formal oversight committee equipped with the relevant authority to review, supervise, investigate and enforce such research and policy.

17) We look to the adoption of recommendations such as those from the American National Bioethics Advisory Commission's guidelines on Ethical Issues in Human Stem Cell Research.[4] These currently include:

a) A public registry of approved protocols and certified ES and EG cell lines,
b) A database linked to the public registry of information submitted by research sponsors that includes all protocols that derive or use ES or EG cell lines.
c) The use of such database to track the history and use of these cell lines for policy assessment and formulation.
d) A report at least annually with an assessment of the current state of the science for both the derivation and use of human ES and EG cells, a review of recent developments in the broad category of stem cell research, a summary of any emerging ethical or social concerns associated with this research, and an analysis of the adequacy and continued appropriateness of the recommendations.
e) Institutional review of protocols to ensure compliance to Human Stem Cell Research Subcommitee / BAC policy.

Conclusion

18) It would appear that the embryo, with a full complement of human genetic material, is not yet capable of rendering consent for experimentation, regardless of the potential benefit to the rest of humanity. It is our hope that we draw the line at this time against embryo research, and reaffirm our societal moral precedent which should consistently support the inherent value of human life, rather than a value which is somehow measured by a simplistic human standard.

19) To quote Dr Dan Brock[5], "While moral and even human rights need not be understood as absolute, that is, as morally requiring people to respect them no matter how great the costs or bad consequences of doing so, they do place moral restrictions on permissible actions that appeal to a mere balance of benefits over harms. For example, the rights of human subjects in research must be respected even if the result is that some potentially beneficial research is made more difficult or cannot be done, and the right of free expression prohibits the silencing of unpopular or even abhorrent views; in Ronald Dworkin's striking formulation, 'rights trump utility'[6]."

20) Philosopher Joel Feinberg[7] has argued for a child's right to an open future. This requires that others raising a child not close off future possibilities that the child would otherwise have, thereby eliminating a reasonable range of opportunities from which the child may choose autonomously to construct his or her own life. We consider this as a basic truth that applies equally to an embryo as to a liveborn infant.

21) It is the nature of a being, not how it is created, that is the source of its value and makes it worthy of respect.

Yours sincerely,

References:

1. *Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine*, Directorate of Legal Affairs, Strasbourg, November 1996, DIR/JUR (96) 14.

2. *Recommendation No. R (90) 3 of the Committee of Ministers to Member States Concerning Medical Research on Human Beings*, adopted by the Committee of Ministers on February 6, 1990, at the 443rd meeting of Ministers' Deputies, (1990) 41 (3) *IDHL* 461.

3. *Recommendation 1100 (1989) on the Use of the Human Embryos and Foetuses in Scientific Research*, in text adopted, Parliamentary Assembly, 40th Session, Party III, a. D. 9. in Appendix.

4. *Ethical Issues in Human Stem Cell Research* National Bioethics Advisory Commission – Executive Summary 1999.

5. *Cloning Human Beings - An Assessment of the Ethical Issues Pro and Con* Commissioned Paper for the National Bioethics Advisory Commission. Dan W. Brock, Ph.D. Brown University 1999

6. *Taking Rights Seriously*, Dworkin, R., London: Duckworth, 1978.

7. *Whose Child? Children's Rights, Parental Authority, and State Power*, Feinberg, J., W. Aiken, H. LaFollette (eds.), Totowa, NJ: Rowman and Littlefield, 1980.

Name: Date:

Opinion for or against
Yes (Y) ,
No (N) ,
No but would not object to others pursuing this research within guidelines (P)

Survey on Stem Cells Issues	**Options - Y, N, P**
1. Animal Cloning	-
Human Stem Cell Research	
2. Adult Stem (AS) Cells Research (bone marrow, umbilical cord blood, brain etc)	-
3. Embryonal Germ (EG) Stem Cells Research (from aborted fetuses)	-
4. Embryonic Stem (ES) Cells Research (Early Embryo <14 days)	-
5. Therapeutic Cloning	-
6. Reproductive Cloning	-
7. Constant need to review policies (on a regular basis in view of rapid development in this area)	Y or N
8. Conscientious Objection to participate in TOP Under Termination of Pregnancy Act	Y or N

SURVEY RESULTS 56 respondents 13/12/2020

ANIMAL CLONING

	Frequency	Percent
n	10	17.9
p	4	7.1
y	42	75
Total	56	100

ADULT STEM CELL

	Frequency	Percent
n	2	3.6
p	2	3.6
y	52	92.9
Total	56	100

EG

	Frequency	Percent
n	8	14.3
p	10	17.9
y	38	67.9
Total	56	100

ES (<14d)

	Frequency	Percent
n	22	39.3
p	9	16.1
y	25	44.6
Total	56	100

Therapeutic Cloning

	Frequency	Percent
n	16	28.6
p	13	23.2
y	27	48.2
Total	56	100

Reproductive Cloning

	Frequency	Percent
n	42	75
p	11	19.6
y	3	5.4
Total	56	100

CONSTANT REVIEW

	Frequency	Percent
n	1	1.8
y	55	98.2
Total	56	100

TOP objection

	Frequency	Percent
n	27	48.2
N.A.	1	1.8
y	28	50
Total	56	100

Practice Location

	Frequency	Percent
Gleneagles Hospital/Medical Centre	7	12.5
KK Women's & Children's Hospital	20	35.7
Mt Elizabeth Medical Centre	7	12.5
National University Hospital	5	8.9
Private O&G Clinics Central & South Zone	8	14.3
Private O&G Clinics East Zone	1	1.8
Singapore General Hospital	5	8.9
Thomson Medical Centre	3	5.4
Total	56	100

		NO OBJECTION		OBJECTION TO TOP	
ANIMAL					
		Frequency	Percent	Frequ	Percent
Valid	n	3	11.1	7	25
	p	2	7.4	2	7.1
	y	22	81.5	19	67.9
	Total	27	100	28	100
ADULT					
		Frequency	Percent	Frequ	Percent
	n	1	3.7	1	3.6
	p			2	7.1
	y	26	96.3	25	89.3
	Total	27	100	28	100
EG					
		Frequency	Percent	Frequ	Percent
	n	3	11.1	5	17.9
	p	4	14.8	6	21.4
	y	20	74.1	17	60.7
	Total	27	100	28	100
ES					
		Frequency	Percent	Frequ	Percent
	n	7	25.9	15	53.6
	p	3	11.1	6	21.4
	y	17	63	7	25
	Total	27	100	28	100
therapeutic					
		Frequency	Percent	Frequ	Percent
	n	5	18.5	11	39.3
	p	4	14.8	8	28.6
	y	18	66.7	9	32.1
	Total	27	100	28	100
reproductive					
		Frequency	Percent	Frequ	Percent
	n	17	63	25	89.3
	p	7	25.9	3	10.7
	y	3	11.1		
	Total	27	100	28	100
REVIEW					
		Frequency	Percent	Frequ	Percent
	n			1	3.6
	y	27	100	27	96.4
	Total			28	100

TOPobject

	Frequency	Percent
n	27	100

Practice Location

	Frequency	Percent
Gleneagles Hospital/Medical	2	7.4
KK Women's & Children's Ho	11	40.7
Mt Elizabeth Medical Centre	3	11.1
National University Hospital	2	7.4
Private O&G Clinics Central &	4	14.8
Singapore General Hospital	3	11.1
Thomson Medical Centre	2	7.4
Total	27	100

TOPobject

	Frequ	Percent
y	28	100

Practice Location

	Frequ	Percent
Gleneagles Hospital/M	5	17.9
KK Women's & Childr	9	32.1
Mt Elizabeth Medical C	4	14.3
National University Ho	2	7.1
Private O&G Clinics C	4	14.3
Private O&G Clinics E	1	3.6
Singapore General Ho	2	7.1
Thomson Medical Cen	1	3.6
Total	28	100

B. RELIGIOUS GROUPS/ORGANISATIONS

The Inter-Religious Organisation of Singapore (submitted under the IRO) obtained views from the Roman Catholics, Bahai faith, Jewish faith, Taoists, Hindus and Sikhs.

1. Hindu Endowments Board *(submitted under the IRO)*
2. Taoist Mission (Singapore) *(submitted under the IRO)*
3. St. Anthony's Canossian Convent *(submitted under the IRO)*
4. Sikh Faith view *(submitted under the IRO)*
5. The Spiritual Assembly of the Baha'is of Singapore Ltd *(submitted under the IRO)*
6. The Jewish Welfare Board *(submitted under the IRO)*
7. Singapore Buddhist Federation
8. The Catholic Medical Guild of Singapore
9. National Council of Churches of Singapore
10. Singapore Council of Christian Churches
11. Majlis Ugama Islam Singapura

HINDU ENDOWMENTS BOARD

397 SERANGOON ROAD, SINGAPORE 218123 TEL: 2963469 FAX: 2929766
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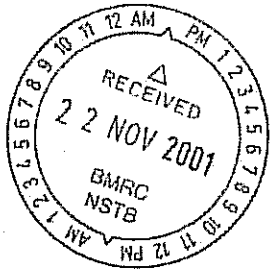
19 November 2001

Prof Lim Pin
Chairman
Bioethics Advisory Committee
250 North Bridge Road
#15-01/02 Raffles City Tower
Singapore 179101



Dear Prof Lim

REQUEST FOR FEEDBACK REGARDING HUMAN STEM CELL RESEARCH IN SINGAPORE

1 We refer to your letter dated 8 November 2001.

2 Energy in the form of life is manifested in the living cells including stem cells derived from early embryos (ES cells).

3 It is suggested that in Singapore the embryos created by invitro fertilisation, not more than 14 days old, can be used for research.

4 So also, the ES cells derived from 5 days old frozen embryos can be used to establish the cell lines.

5 According to our Faith (Hinduism) killing a foetus is a sinful act (BHROONA HATHYA). But whether the 14 days old foetus is endowed with all the qualities of life is not well regarded. Therefore, there is no non-acceptance to use these ES cells to protect human life and to advance life by curing diseases.

6 Another point that needs clarification is whether all the cells in the 14 days old foetus will be completely used since they presumably remain in an undifferentiated state. If this is so the question of killing the foetus would not arise and all the cells would continue to live and function.

7 EG cells are not suitable for research since embryogenic germ cells are derived from foetuses and rest of the foetus or living cells would be destroyed or killed.

8 No objection whatsoever for obtaining some cells from bone marrow and umbilical cord since no killing of the foetus is involved. The process is comparable to organ donation. Instead of organ one would be donating cells.

ESTABLISHMENTS ADMINISTERED

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(A National Monument)
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Tel: 7434506 Fax: 7437622

THE ASHRAM
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Tel: 7539730 Fax: 7533727

SRI SRINIVASA PERUMAL TEMPLE
(A National Monument)
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9 However one major ethical question remains largely unanswered. That is the scientist creates a new form of life (embryo) by using two living cells (sperm and egg)of two different morphological categories derived from two different individuals.

10 Diversity establishes uniformity by process of fertilisastion forming embryo, which differentiates again into polymorphic cells. Life is continuing through out this entire process of cell division and differentiation and that is the marvel of life, The risk of damaging life or killing some cells is always there when cells are separated, grown and used again.

11 The implications involved in the process and saving or maintaining the life factor undamaged throughout needs to be fully discussed before arriving at the final decision.

12 I hope that these views would be useful to the committee for discussion.

Yours sincerely

V R NATHAN
CHAIRMAN

Cc Prof A N Rao, HEB-Religious Affairs Committee

feedbackprofrao

新加坡道教协会
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TAOIST MISSION (SINGAPORE)
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莫以善小無益而不為 莫以惡小無損而為之

谨致：生物道德咨询委员会主席
林彬教授　台鉴，

就关于"管制本地胚胎干细胞的研究工作"课题道教的意见书

道教与其他宗教最大的区别之一,就是对于现世生命的热爱、养护和延益.道教把乐生认为是最善,长生认为是大德.这一种乐生贵生的思想,在道教经典中俯拾皆是.教徒们正是在这种思想的指导之下来思考宇宙、社会与人生的,很必然地便将人放在了心的地位.

道教认为日月星辰及天地万物,包括人,均从道中流衍而出.认定道化生了万物,而且万物又将复归于道.

生死是道教教义重要概念.<<性命圭旨>>论生死大概经过以下几个阶段,即一个循环：死 — 投胎 — 成形 — 成人 — 由幼儿到老人 — 死.即虚化神、神化气、气化血、血化形、形化婴、婴化童、童化少、少化壮、壮化老、老化死、死复化为虚、虚复化为神、神复化为气、气复化为物.化化不间,循环无穷.

吕洞宾所传<<钟吕传道集>>之'论真仙'中云："吕曰：人之生也,安而不病,壮而不老,生而不死,何道可致如此?钟曰:人之生,自父母交会而二气相合,即精血为胎胞,于太初之后而有太质,阴承阳生,气随胎化,三百日形圆,灵光入体,与母分离……".

生道合一,是道教基本教义内容之一.道教继承了中国古代仙学传统,特别重视现世生命的长久存在,追求的最高目标是得道成仙,即所谓"深根固蒂,长生久视"之道.其中的生,即是生命、生存的意思.早期道经<<老子想尔注>>中,即将"道"与"生"并列,尊为四大的内容.<<太上老君内观经>>："道不可见,因生以明之;生不可常,用道以守之.若生亡,则道废,道废则生亡.生道合一,则长生不死."认为"天地构精,万物以生","父母和合,人受其生","从道而生谓之命,自一禀形谓之性",从虚无大道中产生了人的生命.而万物之中,人为最灵,"性命合道,当宝爱之",应该至为爱惜生命的存在.生道合一教义是道教仙学的核心内容,以此为准则,道教采撷、造作了诸多炼养方术,如内丹、存思、守一、服气、辟谷、房中等术,以求达到"生道合一"的目标

道教重生、贵生,故注重养生,认为人生活在世界上是一件乐事,死亡才是痛苦的,因此它的教义是乐生、重生和贵术.强调"仙道贵生,无量度人",因而便寻求能够使人长寿的方法.主张"我命在我,不在天地"的理论,认为人的寿命长短,由自己决定,通过修炼能够延年益寿,甚至长生久视.

道教戒律一直为道教徒修道持身之规范,积功累行之径路.益善止恶,皈真舍妄,莫不由此渐进而顿悟.按:<<老君戒经>>曰:"一切众生,含气以上,翱飞蠕动之类,皆不得杀.蠕动之类无不乐生,自蚊蚁蜉蚴咸知避死也.

道教的立场

道教崇尚自然,道教主张要自然无为.要认识自然的规律,并掌握自然,运用自然,反对有为的作为,违反自然,人为地造作.只要是不违反自然的研究,有益于众生,道教是支持的.

道教是科学的,纵观道教的历史,许多道教的道士,方士都是从事科学的研究,道教特别注重各类的身心炼养术研究,如:守一、存思术,服气、胎息术,房中术,内丹术及养生医学...等.

道教非常珍惜生命,有所谓"仙道贵生,无量度人"的说法.在不伤害其他生命,不违反伦理道德及不违背道教教义,而进行有益于延年益寿,造福人类的研究,道教是支持的.

道教反对在违反自然,杀害其他生命及违背道教教义,如采取胚胎之研究.因此,为避免此研究有被滥用的可能性,站在道教的立场来看待此课题,我们坚决认为政府必须设立法定机构,严格管制本地胚胎干细胞的研究工作.希望我们的意见能给
贵会有所帮助.专此奉达,即颂

大安

福生无量天尊　　此致

新加坡道教协会代会长
道宋李至旺　　稽首
2001年11月28日

Translation of the letter from the Taoist Mission (Singapore), pages G-3-4 and G-3-5

Respectfully Submitted To:
Bioethics Advisory Committee (BAC) Chairman
Prof. Lim Pin

SUGGESTION PAPER PUT UP BY THE TAOIST MISSION (SINGAPORE)
DISCUSSION TOPIC: REGULATING SINGAPORE'S EMBRYONIC STEM CELLS RESEARCH

One of the key differences between Taoism and other religions is its love for and commitment to prolonging and enriching one's present life. In Taoism, "happy living" is considered the highest level of kindness and longevity, the greatest virtue. This kind of ideology of "valuing life" is very common in the Taoist scriptures. According to this teaching, Taoist believers reflect on the universe, human society and philosophy of life. Naturally, they would put mankind at the centre of their thinking.

Taoism believes that the heavenly bodies – the sun, the moon and the stars, and all things in the universe, including men, all emerge from Tao. It is firmly believed that Tao gives birth to all things on earth and that these things will return to Tao eventually.

Life and Death are important concepts in Taoist doctrines. The *Xing Ming Gui Zhi* talks about life and death in terms of the following stages, forming a cycle: death, reincarnation, formation, becoming human, from infant to the aged, and Death. This involves the transformation of Emptiness to Spirit, Spirit to *qi* energy, *qi* energy to blood, blood to shape/form, form into new born infant, new born into child, child into youth, youth into adult, adult into aged, aged into death. Then death returns to Emptiness, emptiness changes once more into Spirit, Sprit into *qi* energy, *qi* energy into things – the transformation is ceaseless and the cycle goes on without end.

In the chapter entitled "Lun zhen xian" (on true immortals), in the *Zhong Lü Chuan Dao Ji* (Collected writings of Masters Zhong and Lü) by Lü Dong Bin, it is reported that Lü asked Master Zhong: "What is the Way that enables a human being to be healthy and not sick, strong and not grow old, live and not die?" Master Zhong replied, "Life comes from the union of the two parents which leads to the union of ying and yang. The essence and blood then form the embryo and with the interaction of yin and yang, the embryo becomes fully formed after 300 days. At that time the spirit enters the body and the new- born leaves the mother's womb.

The unity of Life and Tao is one of the fundamental teachings of Taoism. Taoism inherited China's ancient beliefs in immortality, and especially emphasizes longevity in one's present life. The highest goal in Taoism is to obtain the Tao and become an immortal. This is what is meant by "the Way of living long and having deep and strong roots." The word "living" here means life, existence. The early Taoist text, the *Laozi xiang er zhu* (The Xiang er Commentary on the *Laozi*) has already placed equal emphasis on "Tao" and "life," listing as the content of what the *Laozi* [chapter 25] describes as the "four great ones." Another Taoist text, the *Taishang Laojun neiguanjing* (The Scripture of Inner Vision of the Supreme High Lord Lao) also says, "The Tao cannot be seen, but through life it can be illuminated. Life is never constant; one must use the Tao to guard it. If life ceases, the Tao is lost. If the Tao is lost, life ceases. If life and Tao merge into one, then immortality can be realized." It also states that "heaven and earth form the essence, from which all beings are born"; and "from the harmony and union of one's father and mother, one receives the gift of life." Further, "what is born of Tao is called destiny; and what is shaped by the One is called nature." From the Great Way that is empty human life is created; and among all things, human beings are the highest in terms of spirituality. "The nature and destiny accord with the Tao and should be carefully treasured." This means that one should cherish to the utmost the presence of life. The union of Tao and life is the key doctrine of Taoism. It provides a standard and gives rise to a host of

practices, such as internal alchemy, preservation of pure thoughts, guarding the One, ingesting energy, avoidance of the five cereals, and the arts of the bedchamber, to realize the goal of the union of life and Tao.

Taoism emphasizes life, values life, and as a result it stresses the preservation of one's health. It considers being alive in this world as a pleasure, and death an agony. Thus the teaching of Taoism is to cultivate and nurture life, to value life and to find techniques that enable one to live longer. It stresses that "the way of immortality is to value life, and the highest virtue is to save others." Thus, it seeks to find ways to enable human beings to live long. It stands by the theory that "My life lies in my hand, not in heaven and earth." Whether one's life is long or short, it is determined by oneself. Through the practice of Tao, life can be prolonged and one can even live forever.

The rules and principles of Taoism have been providing Taoist believers with a standard for self-cultivation and a way to accumulate merit through constant practice. Benefit the good and stop evil, follow the truth and discard lies – this is the way that all can make progress and obtain enlightenment. According to *Laojun jiejing*, "All living creatures that breathe, including those that fly and crawl, should not be killed. Even wriggling creatures also treasure life, even mosquitoes and other insects understand the avoidance of death.

Position of Taoism

Taoism values nature. It advocates being natural and opposes aggressive behavior. Recognize the principles of nature, know nature well, apply what is natural, oppose artificial action that goes against nature. Taoism will support researches that are not against nature and are beneficial to all living beings.

Taoism is scientific. Looking at the history of Taoism, many Taoist masters engaged in scientific research. Taoism especially emphasizes various kinds of

practices that cultivate body and mind – for example, guarding the One, preservation of pure thoughts, ingesting energy, embryonic respiration, the arts of the bedchamber, internal alchemy, medical knowledge that prolongs life, etc.

Taoism treasures life deeply. As indicated by the Taoist saying, "the way of immortality is to value life, and the highest virtue is to save others." Provided that it does not injure life, is not against morality and not against the teachings of Taoism, Taoism supports research that increases longevity and brings benefit to mankind.

Taoism is not supportive of research that goes against the teachings of Taoism, that goes against nature, and that involves the killing of another life, e.g. using embryos for research. Thus, from the perspective of Taoism, in order to prevent such research from being abused, the Taoist Mission strongly believes that it is necessary for the government to set up a legislated body to strictly regulate and control embryonic stem cell research work in Singapore."

Mr. Li Zhi Wang
Acting Chairman
Taoist Mission (Singapore)
28 November 2001

Translated by: Christine Ho, NSTB

St. Anthony's Canossian Convent
1604 Bedok North Avenue 4 Singapore 1646
Tel: 4494319

Mr Harbans Singh
Hon. Secretary, I.R.O.
Blk 173 Woodlands Street 13 #02-397
Singapore 730173

24th November 2001

Dear Mr Harbans,

Re: Stem Cell Research – Catholic view

Please find attached a statement published in the Catholic News dated 28th October 2001concerning the Catholic Church's teaching on the subject mentioned above.

The Archdiocesan Bioethics Committee is a committee composed of professional Catholic doctors and they have been entrusted with the task to study and research into question of the stem cell research particularly the embryonic stem cell. The committee has made a careful study on the subject matter taking into consideration the Church's teaching about the sanctity of human life and human embryonic stem-cell research.

The Church's teaching is clear and we do not compromise on our stand. In responding to the Bioethics Advisory Committee, I request that I.R.O.'s submission to the committee will take into full consideration the view offered by the Church.

Thank you for your kind attention.

Yours faithfully,

Sr. Theresa Seow, F.d.C.C.
Consultor of Pontifical Council for Interreligious Dialogue
Catholic Archdiocesan Representative to I.R.O.

c.c. Venerable Shi Ming Yi, Hon. President

Embryonic stem-cell research kills human beings

In response to the issue of embryonic stem cell research which has drawn much attention of late, the Archdiocesan Bioethics Committee is issuing the following statement to clarify what the Church teaches.

What are stem-cells?

Stem-cells are cells that are present in everyone from the moment of conception. These stem-cells give rise to all our other types of cells and all our tissues and organs as we grow and develop in the womb and after birth.

Some of these stem-cells remain in us as adults and they can then be changed into other types of cells, such as blood cells, under the right conditions. These are called adult stem-cells and they can be found in a number of sites, for example in the umbilical cords of newborn babies and in the bone marrow of adults. Adult stem-cells are already being used in new ways of treating diseases such as thalassemia.

Most important of all, obtaining adult stem-cells for research or treatment does not result in the donor being killed or harmed.

But this is not true in the extraction of stem-cells from the human embryo. When this is done, the embryo is inevitably killed.

What is human embryonic stem-cell research and what are stem-cell lines?

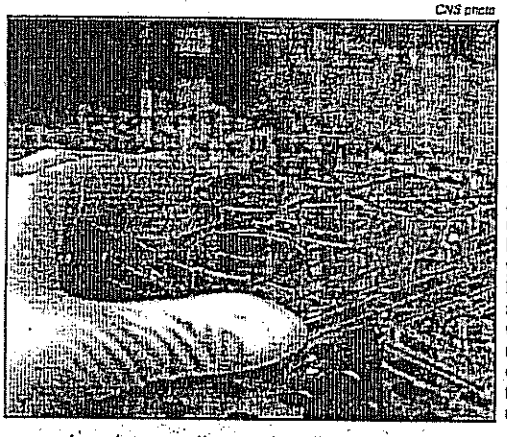
Scientists may extract embryonic stem-cells from either live human embryos produced by artificial reproductive techniques, or specially created by human cloning. After extraction, the cells multiply for prolonged periods in cultures. These are known as cell lines which are then used, sold or exported for further research.

Scientists who do such research hope that products and new methods of treatment may flow from these stem-cell lines. Although the intention of this research may be to find cures for disease, it must be highlighted that live human embryos are killed in the process.

What does the Church teach about the sanctity of human life and human embryonic stem-cell research?

Church teaching regarding human embryonic stem-cell research is consistent with the constant teaching of the Church on the immorality of induced abortion.

CNS photo



A researcher handles culture trays with human embryonic stem cells. A Church document issued last year states it is morally wrong to use human embryos for experimentations.

Since Biblical times, God's divine commandment has been very clear: "You shall not kill" (Ex 20:13, Dt 5:17)

The Church's tradition has always consistently taught the absolute and unchanging value of the commandment, "You shall not kill". It is a known fact that in the first centuries, murder was among the three most serious sins – along with apostasy and adultery. *(Evangelium Vitae, 54)*

Pope John XXIII reaffirmed that human life is sacred because "from its very beginning it directly involves God's creative activity". (*Mater et Magistra*, 1961, 447)

In the encyclical *Evangelium Vitae* (Gospel Of Life), Pope John Paul II said the "evaluation of the morality of abortion is to be applied also to the recent forms of intervention on human embryos which...inevitably involve the killing of those embryos.

"This moral condemnation also regards procedures that exploit living human embryos and foetuses, either to be used as "biological material" or as providers of organs or tissue for transplants in the treatment of certain diseases. The killing of innocent human creatures, even if carried out to help others, constitutes an absolutely unacceptable act." (EV 63)

The Church document *Donum Vitae* (The Gift of Life) states that "from the moment of conception, the life of every human being is to be respected in an absolute way.

"God alone is the Lord of life from its beginning to its end: No one can under any circumstance claim for himself the right directly to destroy an innocent human being." (Introduction, 5)

"To use human embryos or foetuses as the object or instrumentation of experimentation constitutes a crime against their dignity as human beings having a right to the same respect that is due to the child already born and to every human person." (I, 4)

On Aug 25 last year, the Church issued a new document entitled, Declaration On The Production And The Scientific And Therapeutic Use Of Human Embryonic Stem-cells which again stated that it is morally wrong to produce or use living human embryos for the preparation of embryonic stem-cells for the following reasons:

1. The human embryo, from the moment of conception, has a right to its own life, and therefore every intervention which is not in favour of the embryo is an act which violates that right.

2. The ablation of the inner cell mass of the blastocyst, which critically and irremediably damages the human embryo, curtailing its development, is a gravely immoral act and consequently is gravely illicit.

3. No end believed to be good, such as the use of stem-cells for the preparation of other differentiated cells to be used in what looks to be promising therapeutic procedures, can justify an intervention of this kind. A good end does not make right an action which in itself is wrong.

The document further declared, "It is morally wrong to use embryonic stem-cells, and the differentiated cells obtained from them, even if supplied by other researchers or are commercially obtainable, because it entails a proximate material cooperation in the production and manipulation of human embryos on the part of those producing or supplying them."

It is morally wrong to benefit from the evil of human embryonic stem-cell research, even if we ourselves have not done this evil.

The document instead urged "using adult stem-cells to attain the same goals as would be sought with embryonic stem-cells. These applications are undoubtedly a source of great hope for a significant number of suffering people."

Finally, *Donum Vitae* makes this observation: "Science and technology are valuable resources for man when placed at his service and when they promote his integral development for the benefit of all, but they cannot of themselves show the meaning of existence and of human progress." (*Donum Vitae*, Introduction, 2).

Those who would like to read the Pontifical Council For Life's Declaration on Embryonic Stem-Cell Research in its entirety may visit http://www.vatican.va/roman_curia/pontifical_academies/acdlife/documents/rc_pa_acdlife_doc_20000824_cellule-staminali_en.html □

HUMAN STEM CELL RESEARCH
(Sikh Faith View)

The Sikh faith totally respects the sanctity of the Gift of Human Life by God and expects every effort to be made to preserve this stand.

No human being has the right to disturb this natural order or pattern of life's existence. This decision only rests with God. For, it is He who gives life or takes it away as He wills.

> **"By (God's) order, O Nanak! Man comes and goes."**
> **[Adi Granth 13]**

The coming (birth) and going (death) of human beings is at the discretion of God, that is, according to His Will. Any attempt to go against His Divine Will is unethical and also morally wrong.

Human life begins when the male and female living cells unite and God by His word gives life for conception to take place. The human embryo is then formed. Hence, life exists from the very onset.

> ***Placing the soul in the body-cave,***
> ***The Lord began to blow the musical***
> ***Instrument of breath into it.*** ***[Adi Granth 922]***

Therefore, the question of the age of an embryo is merely academic. It does not arise. Any attempt to change this human life pattern is going against Nature and the Will of God. The removal of stem cells from the human embryo kills the embryo in the same way that an abortion does.

Even doctors, when they treat patients cannot claim success unless the God's Grace there.

> ***The assembly of the physicians meets together.***
> ***The medicines become effectual, when the Lord,***
> ***Of Himself, stands amidst them.*** ***[Adi Granth 1363]***

INTER-RELIGIOUS ORGANISATION IRO SINGAPORE

Scientific research may need to continue to prolong life and minimise human suffering. The real danger is in the zeal and enthusiasm of research scientists whose attempt(s) to advance their own study and personal prestige may result in the undesirable cloning of human beings.

> ***Kabir, the physician says, 'I alone am good.***
> ***All medicines are in my power.'***
> ***But, this thing belongs to the Lord***
> ***He takes it away, when He wills.*** ***[Adi Granth 1368]***

There is no objection to the adult AS cells, or EG cells that are derived from human foetuses (due to miscarriage) being used. In regard to ES cells, our view is that human cells are living from the onset of conception and that any form of intervention will kill the embryo in the process.

The destruction of innocent life regardless of the objective of human cell experimentation is not acceptable. It is against the preservation of dignity of human life. Anything that goes against Nature albeit for creation of new life is wrong, both on moral and ethical grounds.

Any attempt or claim to change this natural order by other means is a violation of the sanctity of the Gift of Life, which must always be upheld and respected absolutely.

Gurbaksh Singh Grewal
A Venerable Sikh Devotee
Director Satnam Textiles
B1-19 High Street Centre

Harbans Singh PS
IRO Sikh Faith Representative
Secretary Central Sikh Gurdwara Board

CSGB2001.BAC (Sikh)

新 加 坡 巴 哈 伊 总 灵 体 会
THE SPIRITUAL ASSEMBLY OF THE BAHÁ'ÍS OF SINGAPORE LTD
110-D Wishart Road, Singapore 098733
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Transmitted electronically
30 November 2001

Mr P. Harbans Singh PBM
Hon Secretary
Inter Religious Organisation
Singapore

harbans@singnet.com.sg

Dear Esteemed Sir,

Council Feedback (BAC Request)

We are pleased to attach herewith the reply form and our statement on the question of Human Stem Cell Research in Singapore.

Yours faithfully,
For The Spiritual Assembly of the Bahá'ís of Singapore

William Hui
Secretariat Manager

SIGNED CONFIRMATORY COPY WILL BE SENT BY POST IN DUE COURSE

HUMAN STEM CELL RESEARCH IN SINGAPORE

1. We would like to first express our gratitude to the Inter-Religious Organization in asking us for the Bahá'í perspective on this topic. We have also read the Bioethics Advisory Committee's (BAC) consultation paper regarding human stem cell research locally and the following represent our feedback to the BAC paper.

2. The supreme body of the Bahá'í community worldwide, the Universal House of Justice, has stated that there has been nothing specific in the Bahá'í Writings on subjects such as stem cell research or human cloning. Though the Universal House of Justice has the spiritual authority to make decisions on such previously unaddressed matters, it has in a recent communication stated that it would be premature to currently make judgments on these topics and their spiritual consequences. The House of Justice has thus advised believers who are faced with such questions that they are free to come to their own conclusions based on their knowledge of the Bahá'í teachings on the nature and purpose of life, taking care at the same time not to make dogmatic statements or to offer their individual understandings as standard teaching of the Faith.

3. Below is a brief compilation of pertinent passages from the Bahá'í Writings that indicate the underlying standards that Bahá'ís needs to be mindful of when deciding upon a topic such as human stem cell research.

a) With regard to the soul of man: According to the Bahá'í Teachings the human soul starts with the formation of the human embryo, and continues to develop and pass through endless stages of existence after its separation from the body. Its progress is thus infinite. *(From a letter written on behalf of Shoghi Effendi, 1937)*

b) ... the Bahá'í Writings affirm that the human soul comes into being at the time of conception. However, they do not clearly define the exact biological moment and nature of the event described as "conception" and this may, indeed, be a question that is insoluble by human thought or investigation, since it relates to mysteries of the spiritual world and the nature of the soul itself. *(From a letter written on behalf of the Universal House of Justice, 1997)*

c) The Bahá'í view is very balanced. While appreciating the value of the new medical techniques which enable previously childless couples to enjoy the blessings of a family, the teachings define such limits as are necessary to preserve the dignity of the individual and the sanctity of marriage.

In relation to artificial insemination, the beloved Guardian in a letter written on his behalf to an individual believer states: "... there is no objection to having a baby by means of artificial insemination as long as your husband is the father of it." While artificial insemination is a very different process from in vitro fertilization, the principle enunciated by the Guardian is the same; namely, that to be acceptable to Bahá'ís the egg cell of the wife should be fertilized by the sperm of the husband in the procedure. *(From a letter written on behalf of the Universal House of Justice, 1984)*

d) You have specifically requested information defining the Bahá'í position on the important matter of experimentation with human embryos. It is not practicable for the House of Justice to consider this delicate issue at this time ....*(From a letter written on behalf of the Universal House of Justice, 1990)*

e) Nothing specific has been found in the Bahá'í Writings on genetic engineering. This is therefore a matter on which the House of Justice may have to legislate but the time has not yet come for that. The subject is quite complex, and an informed opinion can be offered only when the scientific understanding is much further advanced than at present and the social implications are clearer. With the emergence of adequate understanding, it will also be opportune to deal with the ethical issues involved. In the meantime, Bahá'ís faced with questions about genetic engineering are free to come to their own conclusions based on their knowledge of the Bahá'í teachings on nature and the purpose of life. However, they should be careful not to make dogmatic statements or offer their own understanding as the teaching of the Faith. *(From a letter written on behalf of the Universal House of Justice, 1997)*

Yours faithfully,
For The Spiritual Assembly of the Bahá'ís of Singapore

Dr. Suresh Sahadevan
Chairman

Notes:

Shoghi Effendi: (1897 – 1957) The Guardian of the Bahá'í Faith after the passing of 'Abdu'l-Bahá in 1921, designated in His Will and Testament as His successor in interpreting Bahá'í writings and as Head of the Faith.

The Universal House of Justice: Head of the Bahá'í Faith after the passing of Shoghi Effendi, and the supreme administrative body ordained by Bahá'u'lláh in the Kitáb-i-Aqdas, His book of laws. The Universal House of Justice is elected every five years by the members of all National Spiritual Assemblies, who gather at an International Convention. The Universal House of Justice was elected for the first time in 1963. It occupied its permanent seat on Mount Carmel in 1983.

'Abdu'l-Bahá: (1844 – 1921) Son of Bahá'u'lláh, designated His successor and authorized interpreter of His writings. 'Abdu'l-Bahá means "Servant of Bahá'u'lláh".

Bahá'u'lláh: Title assumed by Mírzá Husayn-'Alí, Founder of the Bahá'í Faith. Born on 12 November 1817, He declared His mission as the Promised One of All Ages in April 1863 and passed away in Acre ('Akká), Palestine, on 29 May 1892 after forty years of imprisonment, banishment, and house arrest. Bahá'u'lláh's writings are considered by Bahá'ís to be direct revelation from God.

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19 December 2001

Prof. Lim Pin
Bioethics Advisory Committee
250 North Bridge Road
#15-01/02 Raffles City Tower
Singapore 179101

Dear Prof. Lim

REQUEST FOR FEEDBACK REGARDING HUMAN STEM CELL RESEARCH IN SINGAPORE

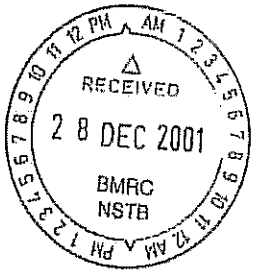
We refer to your letter of 8 November 2001 and reminder of 7 December 2001. Our apologies for not replying earlier as Rabbi M. Abergel is presently on home leave and will return to Singapore in late December. He will revert with his comments.

Thank you.

Yours sincerely

Joseph Benjamin
Honorary Secretary

cc Rabbi M. Abergel



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RABBI MORDECHAI ABERGEL
ORTHODOX JEWISH COMMUNITY OF SINGAPORE

Monday, December 31, 2001

Ms. Lauren Noto
For Prof Lim Pin
BAC Chairman
250 North Bridge Rd.
#15-01/02 Raffles City Tower
Singapore 179101

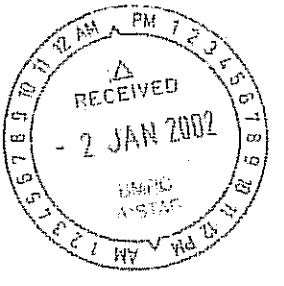
Dear Ms. Noto,

First and foremost I would like to apologize for the delay in our reply. We very much value your interest in the religious aspect of this important issue.

Herewith enclosed is an article which presents the Jewish religious viewpoint. I hope it will answer your request.

Yours Truly,

Rabbi Mordechai Abergel



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Stem Cell Research in Jewish Law

by Daniel Eisenberg, MD

Introduction

Stem cell research is among the most promising and controversial technological breakthroughs of our time. Most cells in the human body are differentiated and, if they maintain the ability to divide at all, have the ability to form only cells similar to themselves. Stem cells have the unique property of being able to divide, while maintaining their totipotent or pluripotent characteristics. Early in mammalian development, stem cells (under the proper conditions) have the ability to differentiate into every cell of the human body (totipotent), potentially forming an entire fetus. Stem cells derived from later stages of mammalian development have the ability to differentiate into multiple cell types, but not into an entire organism. If we were able to manipulate the conditions controlling cellular differentiation, we might be able to create replacement cells and organs, potentially curing illnesses such as diabetes, Alzheimer's disease, and Parkinson's disease.

The ultimate promise of stem cell technology would be to combine it with cloning. Imagine a man dying of liver failure. If we could take a somatic cell from his skin and place the nuclear DNA into a denucleated egg cell, we would have created an almost exact copy[1] of that sick man's cell, capable of differentiating into his clone. Instead of allowing the cloned cell to develop into a fetus, we might place it (or its stem cells alone) into the appropriate environment that would cause it to differentiate into a liver that would be virtually genetically identical to the sick man. If we could "grow" this liver to maturity, we could offer the sick man a liver transplant without the risk of rejection and without the need for anti-rejection drugs.

This sounds like a virtual panacea for many of man's ills. Yet we still do not know if we are able to successfully clone a human, nor are we sure what practical value can be derived from stem cells. We are currently in the realm of fascinating speculation. It will require years of very expensive, labor intensive research to determine the potential that stem cells hold for the treatment, palliation, and cure of human illness. While stem cells have been isolated from adults and aborted fetuses, the best source is the "pre-embryo," the small clump of cells that compose the early zygote only a few days following conception. Therefore, to best investigate the latent possibilities inherent in stem cells, scientists wish to use the approximately 100,000 "excess" frozen pre-embryos that are "left over" from earlier IVF attempts.

What is the *halachic* perspective on such research and what could the possible objections to such research be? There is little argument that the use of stem cells

derived from adult somatic tissue pose few ethical problems. The issues raised by stem cell research involve the use of in vitro fertilized eggs which have not yet been implanted in a woman and the use of tissue from aborted fetuses.

The issues raised by stem cell research may be divided into several questions:
1. Is in vitro fertilization permitted to begin with?
2. What is the Jewish approach to abortion?
3. Are pre-embryos included in the prohibition of abortion?
4. May a very early embryo be sacrificed for stem cells that could save lives or at least cure disease?
5. May we fertilize ova specifically to create an embryo to be sacrificed for stem cells?
6. Need we make "fences" in the form of protective laws to protect fetuses from wanton destruction? May tissue from aborted fetuses be used for research or medical treatment?

In Vitro Fertilization

Artificial insemination has been dealt with a length by a spectrum of *poskim* (rabbis qualified to decide matters of Jewish law). While artificial insemination by a donor is generally strongly condemned, the use of a husband's sperm for artificial insemination in cases of necessity was accepted by most Rabbinical authorities.[2] The question of in vitro fertilization was dealt with later. A significant majority of authorities accepted in vitro fertilization under the same rubric and limitations as artificial insemination,[3] including the fulfillment of the mitzvah of procreation.[4] However, a fundamentally new question arose. What is the status of the "spare" embryos that are not implanted as part of the first cycle of IVF?[5] Must they be implanted in the mother as part of another attempt at pregnancy. May/must they be donated to another women to allow the pre-embryo its chance at life? May they remain frozen indefinitely?[6] Most importantly to our topic, the question arose - may pre-embryos be destroyed? To answer this question, we must first generally examine the Jewish approach to abortion.

Abortion in Jewish Law

The traditional Jewish view of abortion does not fit conveniently into either of the major "camps" in the current American abortion debate. We neither ban abortion completely, nor do we allow indiscriminate abortion "on demand." To gain a clear understanding of when abortion is sanctioned, or even required, and when it is forbidden, requires an appreciation of certain nuances of *halacha* (Jewish law) which govern the status of the fetus.

The easiest way to conceptualize a fetus in *halacha* is to imagine it as a full-fledged human being - but not quite. In most circumstances, the fetus is treated like any other "person." Generally, one may not deliberately harm a fetus, and sanctions are placed upon those who purposefully cause a woman to miscarry. However, when its life comes into direct conflict with an already born person, the

autonomous person's life takes precedence.

It follows from this simple approach that, as a general rule, abortion in Judaism is permitted only if there is a direct threat to the life of the mother by carrying the fetus to term or through the act of childbirth. In such a circumstance, the baby is considered tantamount to a *rodef*, a pursuer after the mother with the intent to kill her. Nevertheless, as explained in the Mishna (Oholos 7:6), if it would be possible to save the mother by maiming the fetus, such as by amputating a limb, abortion would be forbidden. Despite the classification of the fetus as a pursuer, once the baby's head has been delivered, the baby's life is considered equal to the mother's, and we may not choose one life over another, because it is considered as though they are each pursuing the other.

Judaism recognizes psychiatric as well as physical factors in evaluating the potential threat that the fetus poses to the mother. However, the danger posed by the fetus (whether physical or emotional) must be both probable and substantial to justify abortion. The degree of mental illness which must be present to justify termination of a pregnancy is not well established and therefore criteria for permitting abortion in such instances remain controversial.

As a rule, *halacha* does not assign relative values to different lives. Therefore, almost all major *poskim* forbid abortion in cases of abnormalities or deformities found in a fetus. Rabbi Moshe Feinstein, one the greatest *poskim* in this century, rules that even amniocentesis is forbidden if it is performed only to evaluate for birth defects for which the parents might request an abortion. Nevertheless, a test may be performed if a permitted action may result, such as performance of amniocentesis or drawing alpha-fetoprotein levels for improved peripartum or postpartum medical management. While most *poskim* forbid abortion for "defective" fetuses, Rabbi Eliezar Waldenberg (in his *"Tzitz Eliezer,"* vol. 9, chapter 51:3) is a notable exception. Rabbi Waldenberg allows first trimester abortion of a fetus which would be born with a deformity that would cause it to suffer, and termination of a fetus with a lethal fetal defect such as Tay Sachs up to the end of the second trimester of gestation.

The question of abortion in cases of rape, incest, and adultery is a complex one, with various legal justifications propounded on both sides. In cases of rape and incest, a key issue would be the emotional toll exacted from the mother in carrying the fetus to term. The same analysis used in other cases of emotional harm might be applied here. Cases of adultery interject additional considerations into the debate which are beyond the scope of this short article.

In sum, the parameters determining the permissibility of abortion within *halacha* are subtle and complex.

Are Pre-Embryos Included in The Prohibition of Abortion?

While the practical aspects of the Jewish approach to abortion are relatively agreed upon, the exact source and nature of the prohibition is not. Depending on the origin of the prohibition, the application to the pre-embryo will differ. For instance, while most *halachic* authorities consider the prohibition of abortion to be from the Torah, a few consider it to be Rabbinic in nature. It is interesting to note that both the person who performs the abortion as well as the woman who voluntarily allows it to be done are culpable.[7]

The most obvious place to look for the Biblical prohibition would be from the *aseret ha'dibrot* (Ten Commandments), "Thou shalt not murder"[8]. This prohibition, called *retzicha*, usually carries a death penalty for transgression. Nevertheless, it appears the Torah itself teaches that killing a fetus is not equivalent to killing an adult. The Torah specifically states[9] that if in the course of an altercation with a third party, a person causes a woman to miscarry, he pays only monetary damages, while if the woman herself were to die of her injuries, the aggressor would receive a death sentence. Rabbi Yehuda Ashkenazi, in his commentary on the Code of Jewish Law,[10] reasons from here that a fetus is not a full-fledged person, since regarding the one who hits the woman, causing her to miscarry, ". . . he pays the value of the child and we do not label him a murderer, nor do we execute him. . .."

Notwithstanding the statement of Rabbi Ashkenazi, several *poskim* rule that abortion does represent murder, but without the punishment of death.[11] This law is similar to the law of one who kills a *trelfe*[12] (a specific type of terminally ill person), for whom there is a prohibition of murder, but no death penalty.[13] If the pre-embryo is included in this prohibition, then very little short of the pre-embryo posing a threat to someone's life could justify its destruction. An independent threat to the life of a third party would not suffice to allow destroying the pre-embryo.

The argument regarding whether a fetus is included in the prohibition of murder is complicated and fascinating.[14] Both positions garner support from two sides of the same page of the Talmud. Arachin 7a states that the court should strike the abdomen of a pregnant woman to cause a miscarriage prior to her execution.[15] The life of the fetus seems inconsequential in that discussion. On the other hand, Arachin 7b states that the Sabbath may be desecrated for the life of a fetus, something which may only be done to save a life, for *pikuach nefesh*. This apparent contradiction is dealt with at length in the responsic literature.

But is the pre-embryo included in this prohibition? That question is best answered by evaluating the next possible Biblical source for abortion. When Noah and his family exited the ark, G-d commanded them seven laws, which apply to all of humanity. The usual translation of one of these laws is: "Whoever sheds the blood of man, by man shall his blood be shed."[16] The Torah clearly demands capital punishment for murder. While this prohibition appears straightforward, there is a fascinating twist.

The Talmud[17] attempts to prove that non-Jews, who are not obligated by most of the Torah's commandments given at Mount Sinai, are forbidden to perform abortions.[18] The Talmud brings the literal translation of the previously mentioned passage (with slightly altered punctuation), which is: "Whoever sheds the blood of man, within man, his blood shall be shed." It then asks: "What is the meaning of 'man within man'? This can be said to refer to a fetus in its mother's womb." This prohibition, as part of the Noachide laws, would apply to all people, Jew and non-Jew alike, although for technical reasons, the degree of severity would differ.[19]

Once the "standard" prohibition of *retzicha* (murder) is separated from that of killing a fetus, we may investigate how this difference might affect the status of the pre-embryo. From the Talmudic discussion of abortion, we might expect that pre-embryos are not covered by the prohibition of abortion, because they have never been implanted. The rationale for such a decision is based on the concept that a pre-embryo left in its petri dish will die. It is not even potential life until it is implanted in an environment in which it can mature.

Others derive the prohibition of abortion from the Torah's proscription of inflicting damage to one's self or others (*chavala*)[20]. One may not wound one's self without a valid reason (such a medical necessity as in surgery). Obviously, one may not damage someone else.[21] As a result, some claim that the prohibition of abortion arises from the prohibition of the woman wounding herself[22], while others feel that the derivation is from the prohibition of wounding the fetus.[23] Unlike murder, for which only a threat to the mother's life[24] could justify killing the fetus, the rationale of *chavala* allows greater leeway in allowing its abrogation. Particularly, if the wounding of the mother is the prohibition, her consent to being wounded might be considered a determining factor. Whether this prohibition applies to a pre-embryo is open to debate (albeit my personal opinion is that the prohibition of *chavala* does not apply at this level).

The last possible prohibition to consider is the Torah's forbidding of "wasting seed" (*hashchatat zera*).[25] This is the main prohibition involved in questions of male contraception (for example, condoms) as well as the laws governing gathering of sperm for analysis, IVF, or artificial insemination. The prohibition forbids the "useless" emission or destruction of sperm that could create life. Some *halachic* authorities have ruled that excess sperm from fertility treatments may be destroyed. Further, the emission of semen for analysis has been permitted as part of the process of procreation in those suffering from infertility.[26] (Nevertheless, according to most *poskim*, this prohibition does not apply once fertilization has occurred.) Since this ban may be waived for the sake of saving a life,[27] it is conceivable that destroying a pre-embryo to save someone's life (or potentially treat severe illness; this would bring us into the complicated question of "*v'chi omrim lo l'adam chatei bishvil sheyizke chavelrecha*" -- do we allow one to sin in order to save his friend, -- an issue beyond the scope of this article)

would be permitted as part of the mitzvah of *pikuach nefesh*.

Two positive Biblical commandments bear on the obligation to save life (the obligation of *hatzala*). The Torah requires that we "Do not stand idly by as your neighbor's blood is being shed."[28] This *mitzvah* is interpreted by the Talmud[29] to require one to expend positive effort and even money to protect an endangered person. Maimonides learns the whole commandment for a qualified individual to heal his neighbor from the obligation to return lost objects. Regarding a lost object, the Torah commands: ". . . and you should surely restore it to him."[30] From an extra letter in the sentence, Maimonides[31] derives that if one must return a lost object, he must certainly return someone's "lost" health.

Both of these positive commandments may apply regardless of whether there may be any prohibition of abortion for a pre-embryo. But do these positive commandments apply to a pre-embryo? That is, do we have a positive obligation to protect the pre-embryo that is sitting in the freezer?

Forty days

In our analysis, we must also evaluate whether we are more lenient with the destruction of an embryo prior to forty days gestation. There is reason to argue that prior to forty days gestation, the fetus lacks "humanity." The Mishna[32] states that a miscarriage prior to forty days does not cause *tumat leida*.[33] The daughter of a *Cohen* (priest) whose non-Cohen husband has died may continue eating *trumah* (tithes) only if she has no children and is not pregnant. Rav Chisda[34] states that in a case where her non-Cohen husband died soon after marriage, she may continue eating *trumah* for forty days. He reasons that if she is not pregnant, then there is no problem, and that if she is pregnant, that up to forty days the fetus is "*mayim b'alma* (mere water)."

These sources suggest that a fetus prior to forty days gestation is not considered to be an actual person and we might extrapolate that destruction of such a fetus is not forbidden by Jewish law. If we now apply this reasoning to the possible sources for abortion discussed above, we note consistency on the part of the *poskim*.

Rabbi Unterman, former Ashkenazi chief Rabbi of Israel, who ruled that a fetus is protected by the prohibition of murder (*retzicha*), rejects these sources as removing the early embryo from the prohibition of murder. He bolsters his opinion by quoting from Toras Ha'Adam[35], a famous Jewish law book by Nachmanides (Ramban) that discusses medical issues. The Ramban quotes the Ba'al Halachot Gedolot, who asserts that one may desecrate the Sabbath for a fetus because, by desecrating one Sabbath, the fetus will be able to fulfill many Sabbaths in the future.[36] Thus, the Ba'al Halachot Gedolot argues that saving the life a fetus before forty days overrides the Sabbath; therefore, argues Rabbi Unterman, feticide is murder.

Rabbi Yair Bachrach, author of Chavot Yair, does not accept the forty days distinction because he derives the prohibition of feticide from wasting male seed, which is prohibited even before conception.[37]

Rabbi Yosef Trani (author of Responsa Maharit), who argues that abortion is forbidden as *chavala* (wounding) of the mother, does not specifically mention the forty day cutoff. However, Rabbi Yechiel Weinberg (author of the Responsa Seridei Aish), clearly held that there is no prohibition of abortion before forty days according to Rabbi Trani's opinion since there is no "limb" to injure prior to formation of a recognizable fetus at forty days.[38] Rabbi Weinberg himself at first permitted abortion prior to forty days, but later reconsidered his position.[39]

All of the above approaches apply only to Jews who are bound by Torah law. The prohibition of abortion for non-Jews, as discussed above, devolves from the Noachide laws. Of course, non-Jews are forbidden to commit homicide. Yet, according to many commentators, non-Jews are not bound by the commandment in Leviticus 19:16 to protect the lives of their comrades, since it was not commanded to Noah. The scope of their prohibition includes murder and "shedding blood of man within man." These obligations include only actual lives, not potential lives. Therefore, according to Rabbi Unterman,[40] there is no prohibition of abortion for a non-Jew, nor for a Jew to aid in such an abortion, before the fortieth day of gestation.[41]

May a very early embryo be sacrificed for stem cells?

Now that we have analyzed the possible ethical issues in destroying pre-embryos, what is the final outcome? For non-Jews, the issue appears most direct. The combination of the pre-embryo never having existed within a uterus and the generally accepted leniency toward abortion within the first forty days, would strongly argue for a permissive ruling regarding the destruction of pre-embryos for stem cells.

Regarding Jews, the answer is more complicated. Since stem cell research is a new endeavor and cloning of humans has not yet occurred, there are no published responsa on the topic. We must, therefore, look to more practical cases that encompass our question to find an applicable ruling. We find such an issue with respect to the best course of action for couples who wish to avoid having children with Tay Sachs disease when both partners are carriers of the Tay Sachs gene. A similar problem arises in families where the wife carries a gene for a sex-linked disease, such as Fragile-X.[42]

The most promising option for such couples is preimplantation diagnosis, in which a zygote conceived in vitro has a few cells removed to be tested for genetic defects before implantation. Only a zygote that is not homozygous for Tay Sachs or not a male carrier of Fragile-X would be implanted. Rabbi Yosef

Shalom Eliyashuv, possibly the most influention *posek* in Israel today, has permitted preimplantation diagnosis and destruction of affected zygotes to prevent cases of Fragile-X and even in a case of a woman with neurofibromatosis who only had skin lesions.[43] Rabbi Dovid Feinstein has taken a similar view as to the permissibility of discarding "extra" pre-embryos.[44] Pre-implantation diagnosis, which is already accepted by some Rabbinic authorities, is likely to be acceptable to most Jewish legal experts when used to prevent serious diseases in offspring.

Based on these rulings, it would seem that we now have a practical answer to our question of stem cell research. If the pre-embryo may be destroyed, it certainly may be used for research purpose and other life-saving work. In fact, Rabbi Moshe Dovid Tendler, in testimony for the National Bioethics Advisory Commission[45], argued strongly in favor of the use of pre-embryos for stem cell research.[46] Nevertheless, it is important to realize that this conclusion is not unanimous[47] and that all of these rulings are predicated upon the understanding that the pre-embryo is not included in the prohibition of *retzicha* (murder).

May we fertilize ova specifically to create an embryo to be sacrificed for stem cells?

The creation of embryos for the purpose of taking their stem cells is a complex issue. While no responsa yet exist specifically dealing with this question, it is likely that Rabbinic authorities will not favor such a leniency. The mere existence of already created pre-embryos creates a need to decide the *halachic* ramifications of their destruction. We therefore may decide that such research is permitted *bedieved* (*ex post facto*), once the pre-embryos exist. However, since there are *poskim* who forbid abortion even within the first forty days,[48] it is much harder to argue *lichatchila* (*a priori*) that creation of pre-embryos with the intention of destroying them is permitted.

There are additional questions that we as a society must ponder. May we *and should we* deliberately create pre-embryos in order to destroy them?

"Fences" around the law and the use of stem cells and aborted fetal tissue

The Rabbis often create protective edicts (*gezerot*) to prevent the desecration of Torah law. Additionally, the Rabbis may promulgate decrees intended to protect Torah values by preventing untoward behavior that is not already prohibited by the Torah itself. For example, more than 1000 years ago, Rabbenu Gershon enacted *gezerot* banning polygamy and opening the mail of others, despite the absence of actual Torah prohibitions for either of these two actions.

The protection of life is a strongly held Torah ideal. While the destruction of pre-embryos in the course of fertility treatments or to prevent disease may be permitted, this does not mean that pre-embryos may be destroyed without

compunction. To avoid the proverbial "slippery slope," should we ban stem cell research on embryonic stem cells as a dangerous encroachment on the sanctity of life? That is, even if pre-embryos may be destroyed, should we enact preventative laws barring stem cell research that requires the destruction of potential lives to avoid cheapening life by treating the process of creating humans as another scientific process, stripped of its miraculous underpinnings? In his testimony, Rabbi Tendler summed up the issue of protective enactments as follows:

Jewish law consists of biblical and rabbinic legislation. A good deal of rabbinic law consists of erecting fences to protect biblical law. Surely our tradition respects the effort of the Vatican and fundamentalist Christian faiths to erect fences that will protect the biblical prohibition against abortion. But a fence that prevents the cure of fatal diseases must not be erected, for then the loss is greater than the benefit. In the Judeo-biblical legislative tradition, a fence that causes pain and suffering is dismantled. Even biblical law is superseded by the duty to save lives, except for the three cardinal sins of adultery, idolatry, and murder. . . Life saving abortion is a categorical imperative in Jewish biblical law. Mastery of nature for the benefit of those suffering from vital organ failure is an obligation. Human embryonic stem cell research holds that promise. . ..

Human embryonic germ cells may also be derived from gamete ridge tissue removed from first trimester abortuses (at approximately eight-weeks gestation). While abortion of fetuses is a grave offense, it is difficult to justify prohibiting the use of life-saving tissue from these aborted fetuses for fear of encouraging or condoning abortion. This is another case where the cost of a preventative enactment might be the avoidable death of human beings.[49] [50]

Footnotes

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* Dr. Eisenberg resides with his wife and children in Bala Cynwyd, Pa. This article was reviewed for *halachic* accuracy by Rabbi Sholom Kaminetsky of the Talmudical Yeshiva of Philadelphia.

If you have any comments or questions about this article or other medical / *halachic* issues, feel free to contact Dr. Eisenberg at eisenber@pol.net.

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1. While the nuclear DNA would be identical to the donor skin cell, the mitochondrial DNA would be that of the donor egg.

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2. See "Artificial Insemination in Jewish Law," Maimonides: Health in the Jewish World, Vol 5, No. 1, Winter, 1999.

   [BACK]

3. With the important exceptions of (1) Rabbi Ovadia Yosef, who forbids it and rules that it does not fulfill the obligation of fathering children, (2) Tzitz Eliezer XV, no. 45, and (3) Rabbi Moshe Sternbach who denies paternity to the sperm donor and forbids the procedure.

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4. The use of sperm for IVF once the mitzvah of procreation has been fulfilled is more controversial.

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5. See the article by Rabbi Yitzchok Breitowitz, "The Preembryo in Halacha" posted on JLaw.com at http://www.JLaw.com/Articles/preemb.html

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6. The development of cryogenic techniques to freeze pre-embryos only pushed off the crucial question of whether pre-embryos could be destroyed. Prior to cryogenic techniques, several Rabbinic authorities ruled that all fertilized embryos must be implanted. This severely limited the availability of IVF to Torah observant Jews because of the great expense and low yields of each IVF attempt (necessitating fertilization of many ova), and the inherent risk of implanting many embryos. With the advent of cryogenic techniques, many ova could be fertilized with only a few implanted. Nevertheless, the question of disposition of these "frozen" pre-embryos which now number approximately 100,000 remains.

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7. Nishmat Avraham, Orach Chaim 656:1 (p. 92)

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8. Exodus 20:13

[BACK]

9. Exodus 21:22-23

[BACK]

10. Be'er Hetiv, Choshen Mishpat 425:2

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11. See Rabbi I.Y. Unterman, Responsa Shevet M'Yehuda, Vol. I, p. 29 and Noam 6 (1963): 1-11.

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12. A treife is a person with an organic illness that is expected to be fatal within a year.

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13. See Igrot Moshe, Choshen Mishpat II, 69B

[BACK]

14. For more extensive treatment of this debate, see Jewish Ethics and Halakhah For Our Time, Sources and Commentary, Vol. I, by Rabbi Basil F. Herring.

[BACK]

15. To spare her the embarrassment of bleeding during her execution.

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16. Genesis 9:6

[BACK]

17. Sanhedrin 67b: "In the name of Rabbi Yishmael they said: A ben Noach [is liable] even for killing a fetus. What is the reasoning of Rabbi Yishmael? Because it is written [in Genesis 9:6]: 'Whoever sheds the blood of man by man [literally "in man"], his blood shall be shed'. What is the meaning of 'man in man'? This can be said to refer to a fetus in its mother's womb."

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18. Since the Torah was given to the Jews at Mount Sinai, only they are bound by its commands. Nevertheless, all laws given to Noah, the father of all nations, are binding on non-Jews.

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19. Tosofot, Chullin 33a, (d.h. "Echad oveid kochavim"), Tosofot, Sanhedrin 59a (d.h. "Layka")

[BACK]

20. Bava Kamma 90b based on Genesis 9:5 ("the blood of your lives I will surely require"). See Responsa Maharit 97 & 99. See also Responsa Seridei Aish, vol. 3, no. 127 (originally published in Noam 9: 193-215).

[BACK]

21. The laws of damage in *halacha* are extensively discussed in the Torah, Talmud, and codes of Jewish law.

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22. See Responsa Seridei Aish, vol. 3, no. 127 (p. 249)

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23. Rabbi J. David Bleich, Contemporary Halakhic Problems, Vol. 1, p. 341

[BACK]

24. As noted above, the fetus would be classified a *rodef*

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25. See Nida 13b and Responsa Chavot Yair, no. 31. Responsa Sheilot Yaavetz, no. 43 argues that once the sperm has been deposited in the woman, the primary prohibition of *hashchatas zera* no longer applies.

[BACK]

26. Igrot Moshe Even HaEzer I:70, III:14

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27. Generally, all Torah prohibitions except for murder, idolatry, and forbidden sexual relationships are waived to save a human life.

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28. Leviticus 19:16

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29. Sanhedrin 73a

[BACK]

30. Deuteronomy 22:1-2

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31. Maimonides, Commentary on the Mishnah, Nedarim 4:4

[BACK]
32. Nidda 30a

[BACK]
33. *Tumat leida* is the impurity that is created by the birth process, whether live or by miscarriage.

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34. Yevamot 69b

[BACK]
35. Torat HaAdam (in Mosad HaRav Kook Kitvei Haramban, Vol. 2, p. 29)

[BACK]
36. This line of reasoning is brought in Talmud Yoma 85b as one possible reason for why saving a life overrides the Sabbath.

[BACK]
37. See Responsa Sheilot Yaavetz, no. 43, where Rabbi Yaakov Emden argues that "wasting seed" only bars preventing the semen from reaching the woman's uterus. He nevertheless forbids abortion prior to forty days for other reasons.

[BACK]
38. Seridei Aish, vol. 3:350, n.7

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39. Seridei Aish, vol. 3, no. 127 (p. 249)

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40. Responsa Shevet M'Yehuda, Vol. I, 9 and Noam 6:4.

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41. Rabbi Chaim Ozer Grodzinski (Responsa Achiezer, III, 65:14) even entertains the possibility that there may be no Biblical prohibition of abortion before forty days. See also: Tzofnat Paneach 59; Responsa Bet Shlomah, Choshen Mishpat 162; Torat Chesed, Even Ha'ezer, 42:33 all of whom discuss the decreased stringency of abortion within the first forty days.

[BACK]
42. Males with a single gene for a sex-linked disease will be affected by the disease.

[BACK]
43. Personal correspondance with Dr. Avraham Steinberg.

[BACK]
44. Personal correspondance with Rabbi Sholom Kamenetsky.

[BACK]
45. *Stem Cell Research and Therapy: A Judeo-Biblical Perspective*, Ethical Issues in Human Stem Cell Research, Volume III: Religious Perspectives, September 1999, pp.H-3 to H-5. The full text may be downloaded from the National Bioethics Advisory Commission

website at http://bioethics.gov/pubs.html.

[BACK]

46. "The Judeo-biblical tradition does not grant moral status to an embryo before forty days of gestation. Such an embryo has the same moral status as male and female gametes, and its destruction prior to implantation is of the same moral import as the 'wasting of human seed.' After forty days-the time of 'quickening' recognized in common law-the implanted embryo is considered to have humanhood, and its destruction is considered an act of homicide. Thus, there are two prerequisites for the moral status of the embryo as a human being: implantation and forty days of gestational development. The proposition that humanhood begins at zygote formation, even in vitro, is without basis in biblical moral theology." Testimony of Rabbi Moshe Dovid Tendler, Ph.D , *Stem Cell Research and Therapy: A Judeo-Biblical Perspective*, Ethical Issues in Human Stem Cell Research, Volume III: Religious Perspectives, September 1999, p.H-3.

[BACK]

47. E.g., Rabbi J. David Bleich has voiced opposition to the destruction of pre-embryos and their use in stem cell research.

[BACK]

48. Responsa Seridei Aish, vol. 3:350, n.7, Responsa Shevet M'Yehuda, 1;50, Responsa Maharash Engel, 7:85, and Rabbi Moshe Yonah Zweig, Noam 7:48.

[BACK]

49. "In stem cell research and therapy, the moral obligation to save human life, the paramount ethical principle in biblical law, supersedes any concern for lowering the barrier to abortion by making the sin less heinous. Likewise, the expressed concern that this research facilitates human cloning is without merit. First, no reputable research facility is interested in cloning a human, which is not even a distant goal, despite the pluripotency of stem cells. Second, those on the leading edge of stem cell research know that the greater contribution to human welfare will come from replacement of damaged cells and organs by fresh stem cell products, not from cloning. Financial reward and acclaim from the scientific community will come from such therapeutic successes, not from cloning." Testimony of Rabbi Moshe Dovid Tendler, Ph.D., *Stem Cell Research and Therapy: A Judeo-Biblical Perspective* Ethical Issues in Human Stem Cell Research, Volume III: Religious Perspectives, September 1999, p.H-4.

[BACK]

50. Other issues applicable to stem cell research are generic and apply equally to all research. Full informed consent, careful risk-benefit analysis, allocation of scarce resources, and the role of financial gain and renumeration in research have all been dealt with in Jewish law, and are beyond the scope of this article.

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26th November, 2001

Messrs. Bioethics Advisory Committee

250, North Bridge Road
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Singapore 179101

Dear Sirs,

FEEDBACK REGARDING HUMAN STEM CELL RESEARCH IN SINGAPORE

The basic precept of Buddhism is against harming and killing all beings. We are taught to have love and compassion for all beings.

Regarding the research on human stem cell, Buddhism will look at it seriously from the point of intention. If the intention of the research is to find cums specifically to human therapeutic. In other words, if the aim of the research is to help and benefit humankind, then we will deem the research as ethical. On the other hand, if the research is something just for the sake of doing or simply to make money out of it, then we will feel it is unethical.

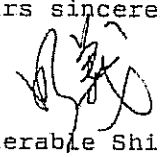
As for human claning, although Buddhism did not state that beings are created by God and the different forms of birth are mentioned in the scriptures, but we are definitely against it. We feel that this will affect the society both morally and socially.

In conclusion, we will support research on human stem cell that will benefit humankind as a result, but are definitely against human claning. We hope the above clarify with the committee the Buddhist stand on human stem cell research in Singapore.

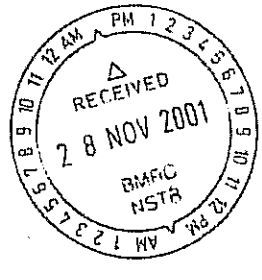
Please feel free to contact us if you have further queries.

Thank you and with best regards,

Yours sincerely,



Venerable Shi Ming Yi
Secretary General---Singapore Buddhist Federation



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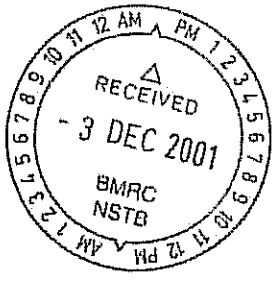

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25th NOVEMBER 2001

Dear Sirs

FEEDBACK REGARDING HUMAN STEM CELL RESEARCH IN SINGAPORE

We refer to Prof Lim Pin's letter dated 8th November 2001, requesting for feedback on the BAC's position on human stem cell research in Singapore.

We would first like to thank the BAC for this invitation for our feedback.

Having read the consultation paper prepared by the Human Stem Cell Research Subcommittee (HSR), we cannot but express our disappointment and disagreement with the HSR's position on research exploiting embryonic stem cells derived from early embryos ('ES cells') and embryonic germ cells obtained from babies killed by induced abortion('EG cells').

We have previously explained our rationale for our opinion in letters to the Deputy Prime Minister, Dr Tony Tan, and the Bioethics Advisory Committee itself, copies of which are enclosed. Together with these, we have also enclosed a copy of the letter sent to the National Medical Ethics Committee by the Archdiocesan Bioethics Commission.

In summary, we would like to put forth the following points:

1. On the basis of a complete biological analysis, the living human embryo is - from the moment of the union of the gametes - a human subject with a well defined identity, which from that point begins its own coordinated, continuous and gradual development, such that at no later stage can it be considered as a simple mass of cells. Jerome Lejeune, who was a professor of fundamental genetics in Paris and a pioneer in detecting chromosomal diseases, once said to a US Senate committee: "Life has a very, very long history but each individual has a very neat beginning, the moment of its conception."

The two moments of real discontinuity in the life of an individual are to be found in the acts of fertilization and of death.

Objections based upon the appearance of the primitive streak and of the nervous system bud, and upon the relevance of the implanting as a decisive event for the continuation of development, do not bear in the least upon the individuality of the embryo or the continuity of development: the appearance of the primitive streak and of the nervous system -- like the whole process of organogenesis -- are the outcome of this active and individualized development. Therefore the objective facts of science tell us that every human being begins life from the moment of conception, or in the case of cloning, when the nucleus of a somatic cell to be cloned is incorporated into an enucleated ovum. It seems painfully apparent that those who have chosen to deny this fact of science have done so in a thinly veiled attempt to justify policies that favour continued experimentation on, and destruction of, our younger and most vulnerable citizens for the sake of material gain.

Put in another way, is it not incoherent to state that a human being begins life only on the fourteenth day after it has already started living (from the moment of conception)?

2. The human being is to be respected and treated as a person from the moment of conception; and therefore from that same moment his rights as a person must be recognized, among which in the first place is the inviolable right of every innocent human being to life.

From this it follows that as a human individual it has the right to its own life; and therefore every intervention which is not in favour of the embryo is an act which violates that right. Therefore, the ablation of the inner cell mass (ICM) of the blastocyst, which critically and irremediably damages the human embryo, curtailing its development, is a gravely immoral act.

In the same vein, every type of therapeutic cloning, which implies producing human embryos and then destroying them in order to obtain stem cells, is immoral.

3. No end believed to be good, such as the use of stem cells for the preparation of other differentiated cells to be used in what look to be promising therapeutic

procedures, can justify an intervention of this kind. A good end does not make right an action which in itself is wrong.
We note that the HSR quite rightly banned reproductive cloning of human beings because it "goes against the moral idea that a human being is not to be treated as a means to an end, but only as an end." It is precisely because of this that a human being, whose life begins at conception, should be given absolute respect at all stages. This respect that is accorded to him should not be made relative to the potential benefit his death may reap for others.

We would like to assure you that the Catholic Medical Guild has no intention of waving aside the potential for good, for curing disease and saving in the name of dogma. On the contrary, we encourage such research for the good of humanity, as in research on adult stem cells and cells obtained from babies that have died from natural abortion (provided adequate informed consent has been obtained). We cannot however condone research on cells obtained from the destruction of embryos and babies killed by induced abortion.

We would therefore like to conclude by stating our unequivocal objection to research that entails the destruction of human life at any stage, because we know that at the end of our lives, we will have to account for what we have done to others at the beginning of theirs.

Yours faithfully

Dr John Hui Keem Peng

Master
The Catholic Medical Guild
of Singapore

Dr John Lee Hew Mun

Immediate Past Master
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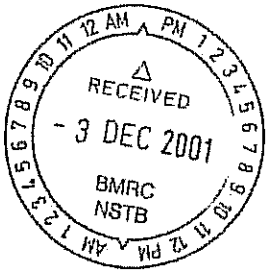

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17th September 2000

Dear Sir,

HUMAN STEM CELL RESEARCH

We are pleased that, in an interview with Channel News Asia on 28th June 2000, you brought up the necessity of a national bio-ethics committee in the future to make sure that our foray into the field of life sciences research is kept within proper ethical boundaries. As health care professionals trained to care for human life from conception to natural death, may we request that such a committee be formed immediately, and that research on human embryonic stem cells be banned, for reasons that follow.

I. **LIFE SCIENCES RESEARCH IS PROGRESSING AT A FAST PACE**
It was first brought to the public's attention in May 2000 that the NUS had been conducting research on stem cells from human embryos less than one week old. On August 11th 2000, it was announced that the EDB, through its investment arm, Life Sciences Investment, would be investing $17 million in a new company, ES Cell International to develop and commercialise a research project on embryonic stem cells by local and foreign scientists.

With this development, research in the life sciences has now gone into full throttle. It is significant to note that it is going on without the existence of a bio-ethics committee to formalise ethical guidelines for such projects. This might undermine your desire to bill Singapore "as a country with practices of high ethical standards in medical research."[1]

II. HUMAN LIFE BEGINS AT CONCEPTION

This is a very important issue, one that will decide our stand on the ethical issues surrounding human embryo research.

Every individual human being begins as a human embryo at fertilisation with the initial fusion of sperm and ovum.[2] In the case of cloning, a new human life begins when genetic material from a somatic cell is fused with an enucleated oocyte.

At fertilisation, the single cell human zygote, in vivo or in vitro, is genetically already a little boy or girl. Immediately, this tiny human being stops his mother's menstrual periods and requiring only shelter and nutrition unilaterally directs his or her own growth and development from a single cell zygote through the 12-16 cell morula and the 5-6 day blastocyst stages until finally setting his own birthday. The blastocyst is never a "pre-human" clump of cells. It is the human embryo, a little human being, that each one of us once was.

III. THE ETHICS OF HUMAN EMBRYONIC STEM CELL RESEARCH

As health professionals, we are convinced that human life must be absolutely respected and protected from the moment of its beginning at conception. In human embryonic stem cell research, pluripotent cells from the inner cell mass of the human embryo at the blastocyst stage are used. In the process the human embryo is destroyed. Such means to achieve the end of excellence in the life sciences can never be justified.

A policy that accords absolute respect to the human embryo is no mere political compromise. It is a reflection of universally accepted ethical principles governing experiments on human subjects – principles reflected in the Nuremberg Code (1947), the World Medical Association's Declaration of Helsinki (1964) and other like documents. Members of the human species who cannot give informed consent for research should not be the subjects of experiments unless they themselves may benefit from it or the experiments carry no significant risk of harm to them. Only by such ethical principles do we avoid treating people as mere means to obtaining knowledge or benefits for others.

IV. WHAT HUMAN EMBRYONIC STEM CELL RESEARCH WILL LEAD TO.

If we accept that there is such a thing as a human life that is not worth protecting at its initial stage of development, it will only be a matter of time before our respect for life at all other stages will be eroded too. If we can experiment with and dispose of a 5-day old embryo, we can do the same with a 2-week, 3-week, or a 5-week old or older embryo.

This is no mere speculation. It has already occurred in Singapore.

At an international symposium on the treatment of Parkinson's Disease held at Singapore General Hospital on 26th August 2000, a local presenter revealed that eight unborn babies had been used at that hospital to treat one patient with Parkinson's Disease. In this procedure, the heads of these babies aborted at six to eight weeks' gestation were taken out whole from their mothers' wombs. Their brains were then dissected and cells were removed from them to be subsequently implanted into the brain of the recipient in a procedure that is still considered experimental.

If unborn children are considered disposable material to be used to treat other "more worthy" human beings or are deemed "useless" or a "burden" to the economy or to the family, there are no further ethical barriers to stop anyone from killing those already born and similarly burdensome, a likely situation in time given the expected increase in the numbers of aged and handicapped.

Again this is no mere conjecture. There is precedent. The Nazi experience and the subsequent Nuremberg medical trials in 1946 revealed previously unthinkable facets of human nature and serve as a chilling reminder of the depths to which even well educated and distinguished men can sink. Starting with the presumption that there is such a thing as a human life not worth living, these doctor-scientists too followed their dream of genetic cleansing by exterminating in turn the mentally handicapped, the physically infirm, the aged and finally the "inferior" ethnic groups.

And this despite the German government being one of the first in the world to install a system of informed consent in human experimentation, after **Albert Neisser** was fined for infecting patients with syphilis without their knowledge or consent in 1898. It is significant that these regulations in 1900 were initiated by government authorities rather than by doctors or research institutions.

In 1931, the Reich government again found it necessary to issue detailed guidelines clearly distinguishing between therapeutic and non-therapeutic research, even setting out some stricter and more detailed precautions than those contained in the much later Nuremberg code and the Declaration of Helsinki.[3]

Notwithstanding these ethically and legally advanced regulations, it is a matter of history how Nazism made it possible from as early as 1933 for about 400 German doctor-scientists, of whom only 23 were indicted, to systematically destroy the fabric of medical decency.[4] Not only did the then Government abrogate its responsibility but it was also guilty of complicity in medical crimes against humanity that the world still finds difficulty in comprehending. In the words of **Hartmut M Hanauske-Abel**, "*In 1933 the convergence of political, scientific, and economic forces dramatically changed the relationship between the medical community and the government. That same convergence is occurring again and must be approached with great caution if medicine is to remain focused on the preservation of physical and medical integrity.*"[4]

Such people and tendencies are not past, never to happen again. They have continued as hitherto low-key threats. For example, the legacies of Nazism and its medical collaborators reached even into the post-war institutions created to prevent recurrence of their crimes - Nazis **Dr Ernst Fromm** and **Professor Dr Hans Joachim Sewering** were members of the World Medical Association which authored the Declaration of Helsinki (1964).

These threats are increasing. According to **Grodin,** the Declaration itself,"*..undermined the primacy of subject consent in the Nuremberg code and replaced it with the paternalistic values of the traditional doctor-patient relationship.*"[5] It was further modified in 1975 and 1983 and even now the USA's FDA is considering allowing placebo trials whether or not it has already approved one or more treatments for the same condition under study, in direct conflict with para II (2) of the Declaration.

As in Germany before the last war, decades of legalised abortion and in-vitro fertilisation and now embryo stem cell research in Singapore and in the world continue to desensitise us to the fact and the inviolability of human life and foreshadow the same outcome. In the USA, despite much talk of human rights, the escalation of abortion to partial birth abortion in 1996 is another stark reminder of how anaesthetised people have become to the baby's humanity.

Not the least consequence of the failure of care and concern for the unborn baby is the crisis of under-population, irremediable by international migration, that the United Nations Population Division predicts will hit first Europe and Japan over the next 50 years, a possibility hitherto denied for decades by most world leaders.[6]

Significantly, the European Parliament voted at Strasbourg on 7 Sep 2000 by a narrow majority against therapeutic cloning, and asked the governments of the European Union "to introduce binding norms that prohibit all forms of research on any type of human cloning in their territory, and provide penal sanctions for any violation." In addition, the document called on the British government to review its stance on the cloning of human embryos.

It is facile to believe that fertility decline is due to development alone. Development removes the economic reasons for having children and leaves only spiritual and other intangible benefits, reasons that have now also been removed by the soul destroying effects of legalised contraception and abortion. Without these reasons, the motivation to have children cannot be restored by a raft of monetary or opportunity incentives. And as physical infertility and infirmity supervene due to the continuation of societal ageing, even the eventual restoration of these values will likely fail to rejuvenate the population. The pressure for euthanasia and human reproductive cloning may then become intolerable.

The possibilities that Science is providing are increasing so rapidly that ethics and laws have not been able to keep up. There is great danger that each and every such additional scientific "success" desensitises us further and makes us more liable and more vulnerable to a cataclysmic end.

With no moral compass, mankind will pay a very high price if it pursues embryo stem cell research claiming that it offers "*great promise to relieve human misery*" without even having a clear understanding or acknowledgement of what it means to be human. Failure to recognise that an individual human being begins at fertilisation or refusal to acknowledge it on the premise that any action is licit if it benefits others opens a Pandora's box of inequity and injustice against those unable to defend themselves.

Concepts such as pragmatism, loosely translated as "what works is good", and democracy or "governance by the majority," despite their undoubted usefulness, are insufficient, even misleading, as moral or ethical surrogates. Since every evil act has some good effects (that's why people do them), the commonly held notion that the moral integrity of an act can be judged solely by its good effects leads to an increasing acceptance of evil acts and to the escalation of evil. Once it is wrongly claimed that harm can be done to a human being in its early existence for the benefit of others, all further barriers to immoral and unethical action can be whittled away just by the further use of reason.

We need instead to actively promote what **Engel** called the scientific-physician, one who espouses and exemplifies humanism in medicine, and on the other hand to identify and neutralise the impostor, the physician-scientist, to whom human beings are mere scientific material whose mysteries are an object of curiosity to be unravelled without flouting those laws of the land, if any, that have kept up with the scientific possibilities. It is as true today as in 1987 when **Engel** observed that "*...there is an elite class of physician-scientist but as yet few fully qualified scientific-physicians.*"[7]

V. VIABLE AND ETHICAL ALTERNATIVES TO HUMAN EMBRYONIC STEM CELL RESEARCH

Recent research suggests that adult stem cells harbour previously unsuspected developmental potential. Adult bone marrow stem cells injected into the circulation of irradiated adult mouse hosts have given rise to new microglia and astroglia in various parts of the brain[8], new skeletal muscle cells[9], and new hepatic oval cells [precursors to differentiated liver cells][10].

More recent research showed that stromal stem cells injected directly into neonatal lateral ventricles could give rise to differentiated astroglia[11], whereas haematopoietic stem cells contributed cells to new muscle fibres, and postnatal muscle stem cells could give rise to blood cells[12,13]. So too work is being done on new growth factors that permit the body to heal itself.

Adult stem cell research is a lot less objectionable from the moral point of view, and appears to offer the same therapeutic possibilities as embryonic stem cell research.

VI. VIABLE AND ETHICAL ALTERNATIVES TO TREATMENT WITH HUMAN EMBRYONIC STEM CELLS

Stem cell transplantation is a generic term covering several different techniques[14]. For example, **allogeneic** transplants of a healthy donor matched for HLA type who may be a family member or an unrelated volunteer were first used to treat congenital immune deficiencies, bone marrow failure, and haematological malignancies and is now used routinely for some non-malignant conditions such as thalassaemia. Haematopoietic stem cells from umbilical cord blood and placental material following delivery or from the bone marrow and peripheral blood are used.

Autologous transplantation of stem cells from the patient's *own* bone marrow or peripheral blood was introduced to rescue the bone marrow of patients due to undergo high dose chemotherapy, and is now increasingly written into protocols for the primary treatment of solid tumours such as breast cancer and neuroblastoma. Autologous transplantation is also used experimentally to treat difficult autoimmune conditions such as systemic sclerosis and as a vehicle for gene therapy.

If we can identify the mechanisms regulating the differentiation of adult stem cells, we would have a viable way to develop many other tissues for autologous transplantation, which does not carry the risk of rejection.

> Knowledge of stem cell transplantation techniques and their clinical application is thus becoming essential for increasing numbers of medical specialists. These methods are inherently moral and are what the scientific community needs to make continuous progress in medicine. **They do not need to destroy human embryos.**

The developments in the life sciences, and how we respond to them as a nation, will tell us much about ourselves and the values that we embrace. The argument that the destruction of embryonic human beings is permissible when it provides sufficient promise of "medical and scientific progress" may yet win the day. If it does, our nation will have taken a tragic step down the long and perilous path that subordinates morality and human life to cold and utilitarian technology.

We have been beneficiaries of the far-sighted policies of a government that has sought only the best for our country and her citizens. We strongly urge you to look into this matter of grave concern and to establish or re-establish a bio-ethics committee immediately.

CONSTITUTION OF BIO-ETHICS COMMITTEE

We propose that the National Medical Ethics Committee under the present chairmanship of Prof. Ong Yong Yau be given wider terms of reference and powers to regulate the ethics of the burgeoning life sciences. The Committee's membership and statutes may need to be re-constituted to fulfil this wider responsibility.

Alternatively, a new bio-ethics committee of doctors, lawyers, ethicists, scientists, the public, and representatives from major religious groups in Singapore be formed under the chairmanship of the Director of Medical Services or the Deputy Director of Medical Services (Professional Standards).

The terms of reference would include

1. reviewing any patent applications linked to bio-technological inventions
2. blocking any patenting of the human body, any of its parts, embryonic stem cells, the embryo or of human cloning.
3. blocking the patenting of the use of human embryos for industrial and commercial purposes.
4. preventing the creation of embryos for research
5. preventing reproductive cloning.
6. ensuring that any research on embryos will not harm them.
7. preventing procedures modifying the foundational genetic identity of human beings
8. blocking genetic research that could be influence by political, economic and military interests
9. ensuring that any research in the life sciences will be undertaken with full respect for human life in all its stages.

It is imperative that none of its members has any involvement or vested interest (financial or professional) in life sciences research. This committee can meet in

public session, or at least be open to feedback from interested members of the public. This committee shall then report to the ministerial committee looking into the life sciences industry, chaired by your good self, and comprising the Ministers for Trade and Industry and for Health.

We are in full support of a life sciences programme that will enhance the quality of life and generate more wealth for Singaporeans. But it is also our ardent hope that, in our quest to excel in the life sciences, the dignity of human life will still be upheld in all its stages of development. In concluding, we would like to remember what Dwight D. Eisenhower once said: "A people that values its privileges above its principles soon loses both".

Thank you very much for your kind attention and your dedicated service to the nation.

DR HUI KEEM PENG JOHN
MASTER
CATHOLIC MEDICAL GUILD
OF SINGAPORE

DR LEE HEW MUN JOHN
IMMEDIATE PAST MASTER
CATHOLIC MEDICAL GUILD
SINGAPORE

Cc Minister for Health
Minister for Trade and Industry
Director of Medical Services

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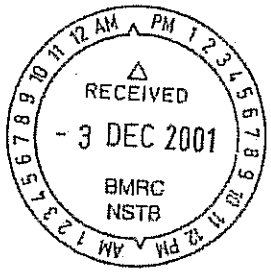

8th October 2001

Dear Sir

Human Embryonic Stem Cell Research

Recent developments in the press and other media on the subject of human embryonic stem cell research have prompted the following further responses from us.

We are highly supportive of the life sciences programme, and are delighted by the government's foresight in developing the "Biopolis", which will certainly help to attract and maintain the top talents in the biomedical sciences. We share in the government's belief that this will help our nation's pursuit of health and wealth. Our support for this includes stem cell research, and the great good for our people that it could result in, with the important exception of research on human embryonic stem cells (HES Cells) and its inseparable killing of human embryos. We have previously focused on this aspect of the life sciences in our letter to Deputy Prime Minister Dr Tony Tan last year.

The following comments are therefore confined to human embryonic stem cell research.

1. **Introduction**
   This is not a debate that we are engaged in but primarily a plea against the unjust taking of innocent human lives, especially among the weak and the voiceless.

Please allow us to elaborate.

2. **The Humanity and Dignity of the Human Embryo.**
First of all, it is a universally accepted fact that the deliberate taking of innocent human life for any reason is beyond debate. The killing of innocent human creatures, even if carried out to help others, constitutes an absolutely unacceptable act.

   The claim that the possible advances in science and medicine are good enough reasons to kill human embryos is seductive, but dangerous as a precedent for future decision making and ethical action.
The question to discuss, if one really exists, is whether or not the human embryo is a human being. And the human embryo is just that.

   He is "human" because he has the human genome and he is a "being" because from the outset he has totipotence, the intrinsic power to develop all his tissues and organs. No cell from human skin or the buccal mucosa fulfils both these criteria. But cloned humans do, which is the primary reason why they may not be created or killed.

3. **On pragmatism as a tool for ethical constructs.**
The principle of pragmatism, loosely translated as "what works is good", is insufficient and misleading, and should not be used as a moral or ethical surrogate.

   In decision making it is first essential to be able to distinguish between acts and their effects. Evil acts are usually committed for their good effects and no sane and free person ever wants an evil result from his evil act. Hence to judge the morality of an act only by its effects is to accept that evil acts are a valid means to an end. Under this principle one may for example try to get rich by any means, fair or foul.

   This is a significant departure from the axiom that crime does not pay and will pave the path to new ways of defining laws and undermine the very core of justice. How for example would a court then treat a plea that there was a good reason for a deliberate murder? In the eyes of the perpetrator there always is.

   A people who believes that good can be obtained through evil are a people who will lose their sense of right from wrong. This degeneration is already obvious in the way that abortion, once a crime, is now a right, and the ease with which the deliberate killing of the human embryo is accepted.

   History is replete with scientists who have done more harm than good, living only for their passion without due regard for the common good. Current scientific literature and the media abound with the exploits of scientists plundering the secrets of unborn humans without concern for their life or welfare and completely disregarding the dignity of babies and ethical concerns of others.

Once we allow the destruction of the human embryo, we will not know when to stop. When we can destroy the embryo at four days for the "greater good" of society, it will be easier to allow the destruction of the embryo at four weeks, then the unborn baby at eight weeks, and so on. One we embark on this path, we will gradually get more and more desensitised to the humanity of our unborn babies. As long as one of us benefits from the death of these babies, it can be justified. It will not be long before this will be extended to the handicapped and aged as our economy in due course feels the strain of looking after the ever-increasing number of aged sick in our midst. Note that pro-euthanasia movements are already very strong in countries that are at the forefront of embryonic stem cell research, namely the United Kingdom and the Netherlands.

Some individuals have tried to justify the destruction of human embryos for research because "they are going to be discarded anyway". The embryo should be treated with as much respect and dignity as any one of us. A convicted murderer who is about to be hanged should not have his organs removed while he is still alive, even if it is for the benefit of others, just because "he is going to die anyway". He is still a human, and deserves respect as such. How we regard embryos perhaps could be extrapolated from how we should regard a child who is found abandoned in the street. We can either try to locate his parents and convince them to take him back, find an adoptive home for him, or if he really is dying, find him a place where he can die with dignity. Any of these solutions sounds plausible. But never dismember him and take out his organs for the benefit of someone else. No one has ever had a right over another's body, but what we do have is a responsibility to care for each other, especially the most vulnerable.

Every embryo destroyed, especially when publicly approved, will weaken our resolve to reduce the already high number of abortions in Singapore. After all, the reasoning is simple: "If the authorities can destroy embryos for society's 'good', why can't I abort my baby for my own 'good' and convenience?"

4. SCIENTIFIC CONCERNS

In a report presented to Congress and the President of the United States in July this year, the NIH conceded that the main problem with embryonic stem cell research was the development of tumours[1]. This fear was well founded, because their scientists found that, when embryonic stem cells were transplanted into mice, some of them turned cancerous. This is not unexpected, given that such stem cells grow almost uncontrollably, and we are far from deciphering the switching on and switching off of cancer genes.

Secondly, the embryonic mouse fibroblast cells that are used as a medium for the growth of embryonic stem cells may be a source of zoonotic infections (infections that are passed from animals to humans), some of

which we may have never encountered, much less been able to diagnose, before. A recent paper presented by a Singapore team involved in such research suggested that they are trying to circumvent this problem by developing a new medium for these cells to grow on. This medium could be of human or synthetic origin. However, this has only been developed in the last six months, is experimental, and is obviously far from perfect. Besides, out of the six cell lines grown so far here, most were developed before the past six months, which means that they have already been exposed to the mouse cells used before. We can never now be too sure if unheard of infections have not already affected these cell lines.

5. **FINANCIAL CONCERNS**

To the extent that financial concerns are tied to ethical concerns over the financial welfare of Singaporeans, we also need to be aware that some problems in embryonic stem cell research might also result in loss of investments.

Among these are the long maturation time of such investments and the risks of therapy such as unknown infections, including zoonotic infections, and the unknown mechanisms involved in the switching on and off of tumour genes.

More important is the increasing opposition to such research in various parts of the world, with the prospect of organisations and governments around the world boycotting products from countries that promote embryonic stem cell research. This cannot be discounted, given the blistering pace at which political structures and events are reshaping the world's political landscape.

Adult stem cell research, which does not involve the destruction of any human being, is progressing at a rapid pace. If a scenario arises whereby a product is developed from adult stem cells at around the same time as one derived from embryonic stem cells, it is almost certain that the former would be preferred.

6. **ON PATIENT CONSENT**

Consent from patients has been offered as a defence to manipulating and destroying human embryonic babies. But to be valid, consent must be **justifiable, informed** and **free**.

"**Justifiable**" means that consent by parents on behalf of their children lacking capacity must be exercised according to the "welfare principle": that the child's "welfare" or "best interests" must be paramount. No parent is ever justified to consent for his child to be given away for prostitution or to be harmed from experimentation. The question is whether consent is in the best interests of the child.

For parents to be "**Informed**" requests need to be transparent. A request like, "Can I have your permission to take your embryo's stem cells? You

should know that he needs these cells to live and will die if I take them" clarifies at least the uncertainty inherent in the current request methods.

Consent must also be "**free.**" Vulnerable patients in a dependent physician-patient relationship cannot give valid consent without fearing that their refusal would interfere with this relationship. "Presumed consent" was criticised by the *World Medical Association* at their 52nd General Assembly in Edinburgh in Oct 2000.[2]

Having a system of "informed consent" therefore does not necessarily imply or guarantee a humane or ethically advanced medical service. It is a sobering thought that Germany was one of the first in the world to have a system of informed consent in 1900 but is now remembered as the world's worst experience of man's inhumanity to man.[3]

7. ON THE NBAC'S ROLE

The decisions of the NBAC as expressed in their final document will have far-reaching effects on the moral and ethical fibre of this nation. The recurring assaults on pre-born babies through abortion, and now by stem cell dismemberment, constitute an unjustifiable attack on the defenceless child.

Will Singapore continue to fail the unborn child because he has no voice? If we choose to follow this course, the precedent set may scar our history forever, and set us on a course of a utilitarian and anti-baby mindset that we may never again recover from. Will we fall prey to the temptation of material riches, or will we pride ourselves as a nation in adopting a more humane and just position?

The adoption and legalisation of practices that are considered unethical and immoral will not dissipate, as is hoped by some, but continue to fester and will flare up again and again each time there is a new way that human babies are mistreated.

We believe that the NBAC will have the wisdom and the courage to confront evil and to map Singapore's advance into the era of life sciences without being unduly influenced by big business or the seduction of science for its own sake rather than man's.

8. ADULT STEM CELL RESEARCH – AN ETHICAL AND VIABLE ALTERNATIVE

Resources for research and development could be directed into more acceptable areas such as the presently under-funded **Cord Blood Bank** and **adult stem cell** research programme. Associate Professor Patrick Tan, Director at the Centre for Transfusion Medicine, recently said that public cord blood banks were worth supporting (ST 24 Sep).

Since it was first reported in Jan 1999 that adult neural stem cells can reinvent themselves as haemopoietic precursors[4, 5], cells of the liver, lung,

gastrointestinal tract, skin, heart and muscle have been grown from adult stem cells. Stem cells from the umbilical cord, placenta, bone marrow, fat and skin can now give rise to cell lines that can treat diseases such as strokes, heart attacks, leukaemia, thalassemia, type I diabetes, and systemic sclerosis, and do not pose the risk of tissue rejection or cause tumours as embryonic stem cells do[6-10].

Just last month, a new adult stem cell identifier ABCG2/Bcrp1 that may be much more specific than the old CD34 standard was reported in Nature Medicine.[11] This could lead to greater harvesting of adult stem cells, increasing its availability for research and therapy. All these possibilities can and should increase rapidly in the near future, given adequate funding and resources.

We hope the NBAC will divert the energies of scientists into these and other more ethical and productive activities. This should not be a major hurdle since scientists do not generally pursue their passion with any premeditated attachment to killing human beings or to offend others. These professionals would on the other hand greatly benefit from sound ethical guidelines and just laws, being able to carry on their work with a clear, well formed conscience. Business interests should take their lumps and learn how to make money ethically, as all entrepreneurs should. Let us not be bankrupt of integrity and honour.

If we do not endorse human embryonic stem cell research, we will not be alone. Germany, Austria, Ireland, Hungary, Poland, Norway, Switzerland and Tunisia are among countries that forbid experimentation on the human embryo.

For example, Germany, chastened and wiser after the experience of its Nazi past, has made it an offence since 1990 to experiment on the human embryo and an offence to possess so-called "spare embryos."[12]

The generation that experienced that holocaust understands the need to stop experimenting on human beings as if they are mere human tissue, and formulated the Nuremberg Code (1947)[13] and the Declaration of Helsinki (1964). In addition, the International Code of Medical Ethics declares that, "A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient."

9. Conclusion

Our wish for Singapore is that we should not just be rich, but also great. It is our ardent hope, therefore, that the **National Bioethics Advisory Committee** will take a positive role as the moral and ethical compass to the life sciences programme. We do not deny that this role is unenviable, and our prayers and best wishes are with you.

This may be our only hope to prevent yet another threat to Singapore's long-term security, prosperity, and fertility – a deepening loss of respect for

the humanity of the unborn child and a widening ethical divide, both local and regional.[14]

We would like to assure you once again that the Catholic Medical Guild has no intention of waving aside the potential for good in the name of dogma. On the contrary, we encourage research for the good of humanity, as in **adult** stem cell research, as long as it does not seek to save some by destroying others, as in **embryonic** stem cell research. When we defend the right to life of every innocent human being – from conception to natural death – as one of the pillars on which every civil society stands, we are simply promoting a human state, a community in fundamental agreement with human nature.

Finally, we recall what Dwight D. Eisenhower once said: "A people that values its privileges above its principles soon loses both". What kind of a people shall we be? The choice is now yours to consider.

Thank you so much for your kind attention.

Yours faithfully

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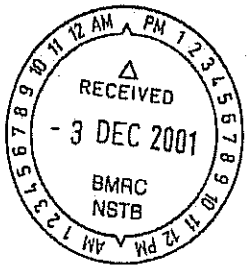

Re: **NMEC Ethical Guidelines for Gene Technology**

1) On behalf of the Catholic Church in Singapore, please allow us to comment on the recent guidelines of the National Medical Ethics Committee (NMEC) entitled, "***Ethical Guidelines for Gene Technology***"

2) The guidelines are a timely reflection of the changing face of medicine and science, and of the increasing needs and wants of the public in this area of medical progress. It is an important area because of the many serious issues effecting researches on the human genome, and the life sciences.

3) It is our opinion that the guidelines are on the whole sufficiently comprehensive and detailed and sufficiently accurate from an ethical perspective to guide the medical and scientific community for the time being, although some amendments and/or clarifications are needed now and in the future as experience is gained.

4) In particular, we have serious reservations to the wording of two entries as presently stated in para 8.2.2(a) and para 9.7 of the guidelines and in para 22 of the summary of recommendations. In our judgement, these are unsatisfactory as they reflect the inadequate practices prevailing with regard to the life of the unborn child.

5) We submit our proposals for changes to these paragraphs for clarity.

6) These important guidelines have been formulated after detailed consideration of the numerous issues relating to the human genome, including important issues such as Human Cloning, and the use of living embryonic stem cells. Thus the guidelines also require the endorsement of the Government of the Republic of Singapore, for if they cannot be enforced, it is as good as not having them. Any professional (e.g. doctors and lawyers) who breaches the professional code of conduct and ethics is subject to disciplinary action. Thus anyone breaching these ethical guidelines must also be subject to disciplinary action.

OUR COMMENTS

7) As stated in the guidelines,
"8 Categories of gene therapy...
8.2.2 We strongly advocate that germ-line therapy with the result of passing on the genetic changes to the offspring should not be contemplated presently for the following reasons:

(a) The ethical issue of whether and when a foetus becomes a patient remains highly controversial. Does the pre-viable foetus have as much an independent right as a patient (subject) as a viable foetus?"

Our comments

7.1 We agree entirely with the NMEC's stand in para 8.2.2 that 'germ-line therapy with the result of passing on the genetic changes to the offspring should not be contemplated'.

7.2 But we are very concerned by the reason given as stated in para 8.2.2(a) which places doubt on the humanness of the baby in-utero. There is no medical or scientific evidence to support the view that the conceptus is at any stage sub-human, pre-human or non-human. As a human being dependent throughout his life in his mother's womb for shelter and nutrition, he is entitled to the care of any patient. Removing this life support is akin to stopping nutrition in an adult who would surely die as a result.

7.3 Worded in the proposed manner in the guidelines, this paragraph is a licence for abortion, foetal experimentation, IVF, trafficking of embryos and embryo spare parts and the sale of human foetal stem cells. Many such abhorrent practices are internationally condemned on ethical and moral grounds.

7.4 For these reasons, the living foetus in the mother's womb is a patient from the time of conception until his birth.

8) As stated in the guidelines,

"9.7 Somatic Gene Therapy in pregnancy.

The introduction of foreign therapeutic gene to the pregnant woman carries a theoretical risk of its inadvertent incorporation into the growing foetus. Such an event, although unlikely with the vector systems used today, is expected to have greater effects on the foetus in the earlier stages of pregnancy, when embryonic organogenesis is actively taking place. *We recommend that somatic gene therapy should be deferred till the last trimester of pregnancy or postpartum unless the perceived benefits of gene therapy to the mother clearly outweigh the risks to the foetus.*"

Our comment

8.1 Introducing foreign therapeutic genes is intended to exert an effect in adult patients who are of course no longer exhibiting organogenesis. Although the very young foetus is at increased risk from these interventions to his mother, the same effects if nor worse may be exerted on him as on the pregnant woman **throughout** intrauterine life, e.g.

8.1.1 When Thalidomide was given to pregnant women (1940s) as a hypnotic drug with no known side effects, it led to the birth of thousands of children without limbs or who had limb defects. This led to considerable suffering for these children and their families for life. Compensation and closure of the company was no expiation for their suffering and for the costs society had to bear for this catastrophe.

8.1.2 Medical Molecular Science is still in its infancy. The functions of many small molecules of proteins, oligonucleosides, and nucleic acids are still unknown. Many of these small protein molecules can cross the placenta and blood brain barrier, and be imbibed and/or endocytosed by totipotential and germinal cells, where intracellular molecular changes may take place. Integration of bacterial proteins are known to take place in the human genome. Natural or synthetic DNA molecules, used for gene or DNA therapy, are often composed of ligands which have bacteria or viral inserts, which can be harmful to the somatic and foetal cells.

One of the major fears of DNA or gene therapy is the induction of carcinogenesis in both somatic tissues and germinal cells in babies in the womb.

For these reasons gene therapy should not be given during ANY stage of pregnancy.

9) The legalisation of abortion and the acceptance of contraception, in particular abortifacient contraceptives, for the last 35 years have dulled the conscience and silenced those who might have sought to protect the unborn child against destruction. And despite the resulting demographic disaster of ageing and death that is surely overtaking the world and the inevitable fate threatening Singapore in about 1-2 decades, no one has yet been able to reverse the decline of fertility for the last 25 years.

10) While the NMEC guidelines cannot adequately counter this threat, they must not propagate further the failure of society to protect the unborn child. The ethic that unborn babies can be killed or maimed to solve social or economic problems must not prevail. In the words of Mr Johannes Rau, President of Germany, "*What is ethically indefensible cannot be permitted for economic reasons.*" He should know. In the aftermath of the world's worst experience of eugenics, euthanasia and selection carried out by a government of an advanced, developed country, Germany banned pre-implantation diagnosis and the use of embryos for research in 1990. This law is still supported by German doctors and by Mr Rau who said, "*Those who begin to instrumentalise human life, to differentiate between worthy of life and unworthy of life are on a runaway train. Nothing may be placed above the dignity of the individual.*"

OUR REASONS

11) Viability assessment is not a philosophical definition for labelling anyone non-human.

The human embryo is capable of independent reproduction and of growing into a developed human form. Viability assessment is a measure of medical management and skill, not a philosophical definition for labelling anyone pre-human, sub-human or non-human. An illustration of the receding frontiers of foetal medicine is the recent example of *Christopher Williams*, who was 16 weeks premature and weighed only 604 grams when he was born in November but who is now, 6 months later, a healthy 4kg in weight.

Furthermore, *Gray's Anatomy*, an internationally acceptable textbook of Human Anatomy and Embryology, has demonstrated that the conceptus has human features at 4 weeks old and that human embryogenesis begins from the time of conception. This definition is accepted by all Human Anatomy Textbooks.

12) Human DNA

Since the time Watson and Crick discovered the structure of human DNA until the present when the structure of the human genome has been unravelled, much information on the human code has accumulated. Yet though the numerous disease associated genes have been identified, much of the functions of the 3 billion oligonucleotides in the genome are still unknown.

13) The human genome is formed in the human zygote

The human genome makes our bodies human bodies and distinguishes a human being from a chimpanzee, a puffer fish and a fruit fly. Each creature has its own distinctive genome that **from the moment it exists** orchestrates its growth and development, determines its structure and function and characterises its status.

14) The totipotent human zygote with its human genome is a living human being

Our human genome formed when each of us originated as a totipotent human zygote co-ordinates our growth and development until we are what we are today. Like the producer and the director, both unfold the story of life **from the moment the covenant is sealed.** From that moment then must the totipotent human embryo with its human genome be accorded the scientific and ethically significant quality of personhood. Hence the dignity of the human person is automatically accorded from the moment of conception.

15) Destroying a zygote that is destined to twin destroys more than one human being

A second arbitrary contention that personhood is absent before the 14th day because of the possibility of twinning before that day is a failure to acknowledge the power of that totipotent human zygote with its human genome to produce not just one but two individuals. Destruction of such a zygote kills more than one human life.

16) The totipotent human embryo is no more a mere collection of cells than we are.

Still others believe that the human embryo is no more than a collection of human cells. If that is true then so is everyone else merely a collection of cells. If we are persons at all, we have been persons since our genome was formed in the totipotent embryo. Whether pearls are in a pile or in a necklace, they are nonetheless pearls. Any seed has the same intrinsic worth as the plant it will grow into - and not because the seed has been genetically modified and patented for profit. To suggest that the embryo has less value than the adult is not to acknowledge the central meaning of embryonic totipotence and the human genome.

17) The totipotent human embryo is a human being and not a *potential* human being.

The human zygote is thus an embryonic human being, possessing all the qualities and power to grow and develop in its natural environment with the addition of only shelter and nutrition until adulthood. Calling the totipotent human embryo with its human genome a potential human person makes as much sense as calling a new motor car under wraps a potential motor car.

18) The sperm cell and the ovum are not potential persons.

On the other hand, it is the human genome that also distinguishes the embryonic human being from a sperm cell and an ovum. The sperm cell and the ovum each has a haploid number of chromosomes and half the DNA complement of somatic cells. Sperm cells deposited in the female genital tract have a maximum life span of about 3 days; an ovum after ovulation a life span of about 24 hours.

After the sperm cell fertilises the ovum, the resulting zygote attains totipotence and a unique complement of human DNA, and when he is placed in his natural environment and his changing needs for growth and development are met, has an expected life span of 75 years until ageing and death. Calling the sperm cell or the ovum a potential human being makes as much sense as calling the hydrogen in the latest zero-emission vehicle potential water, a new entity that has no semblance to it.

OUR PROPOSALS

For all these reasons we therefore propose that para 8.2.2(a) and para 9.7 in the guidelines and para 22 in the summary of recommendations be changed as follows.

19)"8 Categories of gene therapy...

8.2.2 We strongly advocate that germ-line therapy with the result of passing on the genetic changes to the offspring should not be contemplated presently for the following reasons:

(a) All human cells formed from the time of of conception of human parents' sperm and ovum and growing naturally, and sustained in the mother's womb, are living human beings, whose life is sacred from the time of conception. This conceptus shall be accorded the dignity and sanctity of human life. No experiments or procedures whatsoever shall be performed which would be detrimental to the dignity and to the life of the conceptus, which uninterrupted, would result in the birth of the child.

20)"**9.7 Somatic Gene Therapy in pregnancy.**

The introduction of foreign therapeutic genes to the pregnant woman carries a theoretical risk of its inadvertent incorporation into the growing foetus. *We recommend that somatic gene therapy should be deferred till the postpartum period.*"

21)Accompanying the proposal in 8.2.2(a), we propose that para 22 in the summary of recommendations be changed to :

"Summary of recommendations
Recommendations on Somatic Gene Marking and Therapy
22 Somatic gene therapy should be deferred till postpartum."

ALLIED ISSUES

22)**DANGERS OF HUMAN CLONING**

After *Dolly* the first sheep was cloned from the mammary cell of an adult ewe in 1997, scientists cloned other animals within the same breed and also by cross breeding into different species. These successes have emboldened some scientists and clinicians to attempt human cloning now that the procedure has been simplified in animals. What are the dangers of human cloning?

(1) For every *Dolly* that is created there are hundreds of defectives who die or who are aborted, or if they survive have many congenital defects of the heart, lungs and other organs due to DNA damage. Such DNA-damaged persons will pose serious medical and social problems and place a heavy burden on the existing health system. We can also expect that just as foetuses under twenty four weeks are aborted as disposable rubbish, these "less than perfect" human clones could also be thrown into the trash can!!

(2) There have been other serious set backs as *Dolly* did not have the life expectancy of a newborn lamb but died of premature ageing due to unusual telomere shortening that was not present in the normal sheep. Telomere shortening is associated with cell death or premature death.

(3) Even if a human clone survives normally, he would likely be marginalised from a damaged psyche. Although he is a human being like any naturally conceived person, the gods of the human clone will be the machines, incubators and chemicals that gave him life. He can say, "I have no accountability as I am made from a machine or a DNA or the cell of somebody." The desire to help childless couples have their own child or for people to reproduce a dead loved one or for organ transplantation cannot justify the enormous damage to society from thousands of such clones that may be produced in the future. Call to mind also, despite its promise of unlimited energy for the world, how nuclear fission has instead created weapons of mass destruction and caused the expenditure of millions of dollars, leaving less than 10% available for the world's energy needs and for the relief of poverty and famine.
(4) Many international experts, nations, *UNESCO, European Parliament, President Clinton* and now *President Bush*, and Scientists at the Roslin Institute, Edinburgh, have condemned human cloning and have called for a ban on it.

23) LAW ENFORCEMENT & MONITORING.

Without the enforcement of law, there are no penalties for non-compliance. As such, these NMEC guidelines can be flouted with impunity e.g.

Following the NMEC publication (in Feb 2001), several researchers, from the departments of Obstetrics and Gynaecology at the SGH and NUH presented papers at a meeting on the 6 Jun 2001 in the National Cancer Centre on their Stem Cell Research Programme. The presentation was part of a joint proposal for an Institutional Block Grant from the National Medical Research Council to develop the techniques for:

(1) cloning human beings
(2) culturing large quantities of embryonic stem cells
(3) differentiation for tissue engineering (gene therapy)
(4) in-vitro maturation techniques (oocyte maturation & cloning tissue engineering project.)

We are reminded of a lecture at an international symposium on the treatment of *Parkinson's Disease* held at Singapore General Hospital on 26 Aug 2000, where it was revealed that the live brains (embryonic stem cells) of eight aborted babies were used in that hospital to treat a patient with *Parkinson's Disease*. This was subsequently heralded as a great success in the Straits Times on 11 Oct 2000. But reliable studies in the United States since have shown that the condition of some patients who had received these embryonic implants has considerably worsened.

OUR PROPOSAL

(1) Any research grant proposal that incorporates an application to conduct the germ-line research listed above (1-4), which is against the NMEC guidelines, should be rejected by the NMRC and by any other government or government linked funding and regulating body.
(2) Any foreign donation or grant that stipulates the germ-line research listed above (1-4), which is against the NMEC guidelines, should be rejected.

(3) There should be regular (annual, if not more often) inspection of facilities that are conducting research on obstetrical and gynaecological materials to ensure that these guidelines are adhered to. The inspectorate should be given the legal powers to terminate the research there and to withdraw the funding.
(4) These guidelines should be endorsed by the Government of Singapore, and appropriate disciplinary action must be taken against any person(s) who breaches them.

24) We need to actively promote what *Engel* called the scientific-physician, one who espouses and exemplifies humanism in medicine, and on the other hand to identify and neutralise the impostor, the physician-scientist, to whom human beings are mere scientific material whose mysteries are an object of curiosity to be unravelled without flouting those laws of the land, if any, that have kept up with the scientific possibilities. It is as true today as in 1987 when *Engel* observed that "*.there is an elite class of physician-scientist but as yet few fully qualified scientific-physicians.*"

25) The relevant terms of reference of the NMEC and the National Bioethics Committee should therefore include the following:

(1) reviewing any patent applications linked to bio-technological inventions effecting the human genome.
(2) blocking any patenting, and sales of the human body, any of its parts, embryonic stem cells, the embryo, and the human clone.
(3) blocking any funding for the creation of human embryos.
(4) preventing reproductive human cloning
(5) ensuring that any research on embryos will not harm them.
(6) preventing procedures modifying the foundational genetic identity of human beings
(7) blocking genetic research that could be influenced by political, economic and military interests
(8) ensuring that any research in the life sciences will be undertaken with full respect for human life in all its stages.

There should be appropriate penalties for non-compliance.

CONCLUSION

26) Science is at the disposal of Mankind and will give him the power to do immense good or evil. History is replete with examples of both. The seduction of power corrupts and truth itself has become a victim - medical technology is being used equally to save lives and to kill. *Albert Einstein* (1879-1955), himself a scientific giant of the last century, did not mince his words. "*Technological progress*," he said, "*is like an axe in the hands of a pathological criminal.*" Deadly weapons are in the hands of children. If not controlled, science will make victims of us all.

27) It is not that we should become less scientific - we should become more. We must include within medical science the other human sciences and the humanities, such as social science, psychology, philosophy, culture and religion. We have to keep in mind that the purpose of medicine is not only to cure but always to care. Medicine is healing and comforting the sick and doctors have to use their scientific knowledge for the benefit of their patients.

28) We must also have more effective controls. Science needs ethics and a potent NMEC. In the words of *Einstein*, *"Religion without science is lame; science without religion is blind."* It is within the power of the government to provide the moral medical compass and thus regulate the life sciences so that the promise of Science to relieve human misery and have at the same time a clear understanding of what it means to be human is realisable.

29) We sincerely hope that you will consider our constructive criticisms favourably. These were made in the spirit of Humanism and Science and we are guided by the knowledge that all wonderful gifts given to Mankind are for the benefit and the well being of humanity.

DR.JOHN LEE
CHAIRMAN,
ARCHDIOCESE BIOETHICS COUNCIL
SINGAPORE

DR. GABRIEL OON CHONG JIN
MEMBER

cc
DPM (Dr. Tony Tan)
Minister for Health (Mr Lim Hng Kiang)
Minister for Trade & Industry (BG George Yeo)
Director of Medical Services (Prof Tan Chorh Chuan)
Chairman, Biomedical Research Council (Prof. Louis Lim)
Administrator of the Archdiocese of Singapore

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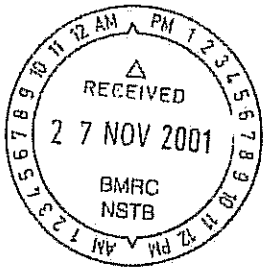

27 November 2001

Prof Lim Pin
Chairman
Bioethics Advisory Committee
250 North Bridge Road
#15-01/02 Raffles City Tower
Singapore 179101

Dear Prof Lim

We refer to your letter dated 8 November to some of us inviting us to send responses to the attached document on Human Stem Cell Research in Singapore.

We wish to thank you for asking for our feedback.

Our denominations are members of the National Council of Churches in Singapore (NCCS). NCCS appointed a Life Sciences Study Group earlier this year to study the ethical issues related to the life sciences. This group comprises scientists, medical doctors, theologians, and ethicists. It has helped us prepare the attached document which is our joint feedback to you.

Besides the denominations we represent, many other churches and Christian organisations are also members of NCCS. The attached response represents our position. We trust that it will receive careful and serious consideration.

Thank you.

Yours sincerely

Bishop John Tan (Lutheran)
NCCS President

Bishop Robert Solomon (Methodist)
1st. Vice President (NCCS)

Bishop John Chew (Anglican)

Rt. Rev. Tan Kheng Hock (Presbyterian)
2nd Vice President (NCCS)

Feedback On Human Stem Cell Research in Singapore

presented by the National Council of Churches, Singapore
to the Bioethics Advisory Committee

Introduction

This document, prepared by the National Council of Churches, Singapore (NCCS), serves as a response to the request for feedback made by the Bioethics Advisory Committee (BAC) on the issue of human stem cell research in Singapore. While there are other related ethical issues not dealt with by the BAC document, our comments focus on matters covered in that document. The NCCS would like to express our appreciation to the BAC for requesting feedback from us.

The NCCS represents the mainline Protestant denominations and other member churches and Christian organisations in Singapore.

Science and the Christian Faith

It must be said at the outset that the best of Christian Tradition supports the development of science in general, and medical science in particular. The scientific enterprise can be seen as an exercise of stewardship, which is a responsibility that is entrusted upon humankind by its Creator. Scientific knowledge and advancement may be seen as instantiations of the divine grace. Furthermore, the healing of the sick and the alleviation of human suffering have always been an integral part of the Christian tradition. The Christian ethic of love compels the Church to engage thus with the world. Medical science, insofar as it is directed towards compassionate healing and treatment, is understood as God's gift to humankind.

The theology of grace that shaped the Christian tradition's attitude towards science is always tempered by a theology of sin. Like all other aspects of human culture, the scientific enterprise can either be an instantiation of divine grace or the vehicle for the expression of human sinfulness. Science has undoubtedly contributed to the betterment of humankind. But history tells us that science has also been used to harm humans as well. The scientific enterprise is tainted by sinful aspirations for glory and economic gain. Science can be conducted in an inhumane manner, even when its goals are noble. For this reason, the Christian tradition has always insisted on the need for ethical parameters to govern scientific activity. For the Christian Tradition, these ethical boundaries must be established on theological grounds, and not just on 'humanitarian' ones.

Embryonic Stem Cell Research

The statements in the previous section are extremely important, for they provide the basis for our comments on specific topics addressed in the BAC document. We agree that much mileage can be achieved through research in AS cells, and that stem cell research should focus on this and other sources. We applaud the BAC's view that 'reproductive cloning of human beings should not be permitted', and agree with the moral view there expressed that the 'human being is not to be treated as a means to an end, but only as an end'. While we share the view that the possible benefit of reproductive cloning for the treatment of infertility 'is greatly outweighed by ethical concerns and safety issues', we maintain that cloning of human beings should be banned unequivocally and not merely on account of the 'high risk of foetal abnormalities'. The latter suggests that human cloning might be envisaged if and when health risks are removed through further refinement in the science of cloning. We applaud the BAC for working on the principle that ethical considerations be placed above therapeutic potentials. We shall urge that the same principle be applied to embryonic stem (ES) cell research.

The ethical concerns surrounding ES cell or EG cell research centres on the status of the embryo. The question is : Is the embryo a human being? And if it is a human being, is it also a person? Our reply to these questions, based on Scripture and tradition, is as follows:

1. Although the Bible does not answer this question directly, the overall thrust of its testimony is that God is the Author and Creator of life and that the beginning of human life cannot be reduced to merely a biological process. God is involved. Every human beginning is part of the divine plan and the result of divine agency. We affirm with the Bible that from its earliest beginning, the human person is valued by God and stands in relation to him.
2. The doctrine of the Incarnation tells us that the Second Person of the Trinity was incarnated in human flesh at conception. At conception, the zygote is already the incarnation of the Eternal Son of God, thereby giving credence to the view that human life begins at conception.
3. The Bible and Christian tradition also make it very clear that the embryo or fetus is a human being – and because it is a human being, it is also a bearer of God's image. The Bible does not make a distinction between a 'human being' and a 'person' in the sense that it is possible for a being to be human but not a person. The human being *is* a person.
4. Both science and philosophy may be said to support this view of the human being. From the standpoint of science, the zygote is already endowed with its own genetic code, and its human nature. We affirm that the embryo from conception is already a human person and are not persuaded that it undergoes any metaphysical change after the fourteenth day that renders a non-human pre-embryo into a human embryo. From a philosophical standpoint, it must be argued that the zygote of human parentage cannot articulate itself into another animal. This is because the zygote of human parentage is already a human being sharing in the nature of its parents.

The BAC's position regarding EG cell research is established on the supposition that it introduces 'no new ethical issues' so long as 'the decision to abort is taken separately and independently from the decision and consent to extract the EG cells'. The issues of abortion and EG cell research are inseparable, and this response must deal with the former in order to address the latter. Because the embryo or fetus is a human being, made in the image of God, its destruction is tantamount to the killing of innocent lives. We cannot countenance the destruction of a fetus even in the context of legalised elective abortion. By implication we do not countenance the use of abortuses for EG cell research, except in the case of fetuses that have been spontaneously aborted, in which case, human intentionality does not come into play. The same logic applies to the use of excess embryos that were created *in vitro*. The fact that we are not responsible for their creation does not give us the liberty to use them for scientific research.

In the same vein, we must voice our objection to what the BAC has termed as human 'therapeutic cloning'. The United Kingdom's Human Fertilisation and Embryology Authority (HFEA) holds that the embryo becomes a human being only at day 14 when 'individuation' occurs. Suffice to say that this opinion is not without detractors even among embryologists. For reasons already discussed, we do not subscribe to this view, but maintain that animation or hominization is immediate rather than delayed, and that there is no window between fertilisation and human conception such that an embryo may be said to be a potential rather than an actual human being. For this reason, we cannot agree to 'therapeutic cloning' which involves the deliberate creation of embryos by nuclear transfer for the purpose of harvesting stem cells, which necessarily entails their destruction. The question of human dignity becomes pressing here. Human beings should not be 'created' merely for use in scientific experiments and disposed. To quote the words of the BAC document – which in our view can be applied here with equal forcefulness and relevance – this procedure 'goes against the moral idea that the human being is not to be treated as a means to an end, but only as an end'.

As far as experimentation with embryo that necessitates their destruction is concerned, it is our considered opinion that the ethical concerns far outweigh the therapeutic potentials. On this matter, we urge the BAC to apply the principle it has articulated so clearly with respect to reproductive cloning, vis-à-vis that human beings must never be treated as means to an end, even if the rationale is scientific progress. The refusal to allow scientific progress to overshadow concerns for human life is found not only in the Christian community, but also in the collective wisdom of humankind as a whole, a wisdom born out of immense struggles in history. In the shadow of Nazism, The Nuremberg Code declared that 'no experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur'. In 1975, the Helsinki Declaration of the World Medical Association maintains that 'concern for the interest of the subject must always prevail over the interest of science and society'.

Recommendations

Based on the above considerations, the NCCS wishes to recommend that the BAC advise the Government to permit and invest only in those Stem Cell Research strategies that do not involve the destruction of human embryos. Cell lines developed from adult marrow and from umbilical cord blood can provide ample material for stem cell research without destroying human life. Stem cells taken from dead fetuses that result from miscarriages can also be used to benefit research. Granted that adult stem cells and stem cells derived from spontaneous miscarriages are not as 'highly proliferative' and malleable as embryonic stem cells, they nevertheless represent a viable alternative to the destruction of human embryos. The refusal to use embryonic stem cell may delay or render more difficult the realisation of the full therapeutic potential of human stem cell research, but it would be a price worth paying since it leads us away from the quagmire of doing harm to innocent lives. By so doing, one is to uphold the two ethical commitments articulated in the BAC statement: 'to protect human life and to advance human life by curing disease'. It should be clear from this statement that the NCCS supports and encourages all stem cell research so long as they do not result in the killing of human embryos. The therapeutic potentials of ES cell research can never outweigh the ethical concerns.

Prepared by
The Life Sciences Study Group
National Council of Churches in Singapore

SINGAPORE COUNCIL OF CHRISTIAN CHURCHES

新加坡基督教联合会

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19 November 2001

Professor Lim Pin
Chairman, Bioethics Advisory Committee
via www.bioethics-singapore.org

Dear Professor Lim

BIOMEDICAL RESEARCH

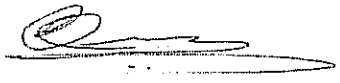
In response to your invitation to the public to voice their views on the subject above (November 18, 2001 : THE SUNDAY TIMES page 5 "Govt Biomedical Watchdog Body May Be Set Up"), may I submit a statement on "STEM CELL RESEARCH" adopted by our church council – the "Singapore Council of Christian Churches" in its 45th Annual General Meeting held on 27 October 2001.

2 The Singapore Council of Christian Church (SCCC) registered under the Societies Act in 1956 bearing registration number R of S REL No 259/56, was the first public body to testify before the Parliamentary Select Committee in 1990 in support of the Maintenance of Religious Harmony Bill (full recordings in the Singapore Parliament HANSARD).

3 SCCC President is Dr Lee Soon Tai, Orthopaedic Specialist, MchOrth (Livp), MBBS (Singapore), FRCS (Glasgow), FRCS (Edin.) FAMS, Med (Surgery). In his voluntary work, he has been serving for many years as Medical Director of Ling Kwang Home for Senior Citizens, Bishan Home for the Intellectually Disabled, Christian Home for the Aged and Ju Eng Home for Senior Citizens. In the event of his personal attendance being needed in any meeting you may be calling to gather feedbacks from the public, Dr Lee will represent our Council.

Thank you.

Yours sincerely



Rev Dr Quek Kiok Chiang, PBM
Vice- President

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STATEMENT NO. 3
ON STEM CELL RESEARCH

The Singapore Council of Christian Churches, meeting on 27th October on the occasion of Reformation Rally 2001 in commemoration of the 484th Anniversary of the 16th Century Reformation, maintains that life begins at the time of conception when the spermatozoan fuses with the ovum. We believe that when Scripture mentions the unborn, the context is almost always one of God's protection for them and His vision for their lives (Psalm 139:13-17 "...Thou hast covered me in my mother's womb"; "Thine eyes did see my substance, yet being unperfect..."; Isaiah 44:1-2 "Thus saith the Lord that made thee, and formed thee from the womb..."; Jeremiah 1:5 "Before I formed thee in the belly, I knew thee; and before thou camest forth out of the womb I sanctified thee...). Human dignity arises from our being created in the image of God.

Whereas, stem cell research is a new frontier in medical science where scientists have succeeded in isolating and culturing stem cells from human embryos, from which body organs are developed and have the ability to grow into the 250 types of tissue in the human body and may hold tremendous promise for treating such conditions as heart disease, cancer and diabetes;

The Singapore Council of Christian Churches opposes stem cell research using human embryos. In order for scientists to isolate and culture embryonic stem cells, a living, human embryo must be killed. It is never morally or ethically justified to kill one human being in order to help benefit another. By requiring the destruction of embryos, the tiniest human beings, embryonic stem cell research violates the Scriptural teaching to preserve life. (Exodus 20:13)

However, opposing the wilful destruction of human embryos for medical research does not mean that stem cell research cannot proceed. The Singapore Council of Christian Churches encourages scientists to continue to explore stem cells found in adult tissues, bone marrow and umbilical cord blood. Initial research using these sources are considered to be very promising, even more promising in some instances than embryonic stem cell sources. (See Appendix on Page 6)

As Christians, we should wholly affirm the desire to develop new treatments for diseases and should vigorously support research into adult stem cells and other non-embryonic sources.

APPENDIX
TO SCCC STATEMENT NO. 3 ON
STEM CELL RESEARCH

An excerpt from the article below gave evidence of the distinct advantages of using adult bone marrow stem cells instead of embryonic stem cell.

A Center for Bioethics and Human Dignity Paper

Cloning and Stem Cell Research Wrong Motives on Both Sides of the Atlantic

"The area of stem cell research has been marked by many unprecedented advances. Ironically, the day before the Donaldson Report was released, the Journal of Neuroscience Research published a study demonstrating that stem cells taken from adult bone marrow had been transformed into nerve cells. This was previously believed to be impossible. Other long-held beliefs, such as the idea that the brain was incapable of regeneration, are being overturned because of research on stem cells derived from non-embryonic sources. With each passing month, research with these stem cells is revealing the huge potential of this area. The hopes of alleviating many devastating illnesses may be achieved via methods which are not dependent upon embryonic stem cells and which therefore do not require the destruction of embryos. As Christians, we should wholly affirm the desire to develop new treatments for diseases and should vigorously support research into adult stem cells and other non-embryonic sources."

Donal O'Mathuna – Mount Carmel College of Nursing

Published in Dignity. Fall, 2000

The national body in Singapore of the International Council
of Christian Churches "for the Word of God and for the testimony of Jesus Christ"

مجلس اكام اسلام سيغافورا
Majlis Ugama Islam Singapura
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28 Nov 2001

Prof Lim Pin
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Bioethics Advisory Committee
250 North Bridge Road
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Singapore 179101

Dear Prof Lim

REQUEST FOR FEEDBACK REGARDING HUMAN STEM CELL RESEARCH IN SINGAPOE

We refer to your letter of 8 November 2001 on the above.

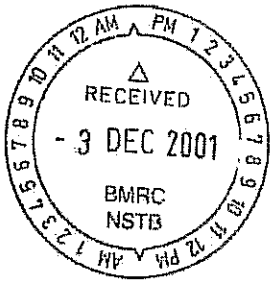
2 The issue had been discussed by the Legal (*Fatwa*) Committee of the Majlis Ugama Islam Singapura which issues *fatwa* (ruling) in matters pertaining to Islamic Law.

3 The Fatwa Committee rules that the opinion of the Bioethics Advisory Committee to use stem cells from embryos below 14 days old for the purpose of research, which will benefit mankind, is allowed in Islam. This is with the condition that it is not misused for the purpose of human reproductive cloning, which would result in contamination of progeny and the loss of human dignity.

4 The full text of the said ruling and its English Translation are attached.

Yours sincerely

HJ MAAROF SALLEH
PRESIDENT
MAJLIS UGAMA ISLAM SINGAPURA



MAJLIS UGAMA ISLAM SINGAPURA
MESYUARAT KHAS
JAWATANKUASA FATWA 2001 – 2004
KHAMIS 22, NOVENBER 2001

- **Pendahuluan**

Jawatankuasa Penasihat Bioetika (BAC) telah mengeluarkan pendapat menerima penggunaan embryo (janin) yang telah disemai di luar rahim wanita mengikut kaedah *in-vitro fertilisation* (penyemaian benih) yang berusia tidak lebih daripada 14 hari, bagi tujuan kerja-kerja penyelidikan berhubung sel induk yang dapat memanfaatkan manusia.

Berdasar kajian saintifik yang telah dilakukan, embryo yang belum mencapai 14 hari tidak dapat merasa sakit kerana hanya pada hari ke 14 satu jalur asli muncul dan berkembang untuk menjadi sistem urat saraf.

Jawatankuasa Fatwa telah diminta memberikan fatwanya dalam isu ini dan hal yang berkaitan dengannya.

Sebelum ini, Muis telah mengadakan ceramah pada 8 September 2001 mengenai Sel Induk dan genom (Stem cell and genome) yang disampaikan Professor Madya Tusqa Too Heng Poon. Ceramah ini dihadiri oleh anggota Majlis Tertinggi Muis dan anggota Jawatankuasa Fatwa Muis.

- **Garis pandu Syarak**

Daripada penerangan tersebut dan pengkajian dalam isu ini, Jawatankuasa Fatwa berpendapat bahawa dasar agama Islam mengalu-alukan penyelidikan ilmiah termasuk yang bersangkut-paut dengan genom manusia, kejuruteraan baka dan seumpamanya. Apa yang diharapkan ialah penyelidikan tersebut dapat digunakan untuk maslahah (kepentingan) manusia bagi merawat penyakit-penyakit yang dihadapi manusia. Sejauh mana penyelidikan dan perlaksanaannya dilakukan hendaklah berlandaskan kaedah fiqh yang muktabar seperti :

a) "لا ضرر ولا ضرار"
Ertinya :
" Tidak ada kemudaratan dan tidak boleh berbuat hal yang memudaratkan".

Maksud kaedah ini ialah :

i. Jangan melakukan kemudaratan kepada diri sendiri dan kepada orang lain, atau

ii. Jangan melakukan sesuatu yang berguna pada diri sendiri, tetapi mendatang kemudaratan atau kesusahan kepada orang lain.

b) " الضرر يزال"
Ertinya : *"Kemudaratan hendaklah dihindarkan"*
Maksud kaedah ini ialah : Sesuatu mudarat jika yakin akan berlaku, hendaklah dihindari sama ada sebelum atau sesudah berlaku.

- **Kedudukan Janin Menurut Syarak**

Apakah pandangan Syarak mengenai janin yang disenyawakan sama ada di dalam atau luar rahim?

Jawatankuasa Fatwa berpendapat bahawa Syarak tidak menetapkan apa jua hukum ke atas janin yang belum terbentuk, lebih-lebih lagi jika ia masih lagi di peringkat embryo. Janin pada hakikatnya dikira bernyawa setelah ditiup roh padanya, iaitu setelah ia berusia empat bulan. Inilah pendapat yang dipegang oleh kebanyakan fuqaha, berpandukan hadis Abdullah bin Mas'ud :

"إن أحدكم يجمع خلقه في بطن أمه أربعين يوما ثم يكون في ذلك علقة مثل ذلك ثم يكون في ذلك مضغة مثل ذلك ثم يرسل الملك فينفخ فيه الروح ويؤمر بأربع كلمات بكتب رزقه وأجله وعمله وشقي أو سعيد"

Ertinya : *"Sesungguhnya setiap kamu diciptakan kejadiannya dalam perut ibunya selama 40 hari air mani, kemudian menjadi segumpal darah seperti demikian itu, kemudian jadi seketul daging seperti yang demikian juga, iaitu 40 hari, kemudian diutuskan kepadanya malaikat lalu diitup roh padanya dan diperintahkannya menulis empat kalimat, iaitu rezekinya, umurnya, amalnya dan celaka atau bahagia."* Muttafaqun 'Alaihi.

Oleh yang demikian, janin yang berusia kurang empat bulan tidak kira sama ada di dalam atau di luar rahim, dianggap hidup berdasarkan keadaannya dalam peringkat proses pembenihan atau pembudidayaan. Ia belum lagi dianggap sebagai suatu permulaan kehidupan yang diukur dengan wujudnya roh.

Pandangan serupa ini telah pun diutarakan oleh para fuqaha dahulu dan masa kini, antara mereka ialah Dr Muhammad Sulaiman Al-Asyqar yang memberikan pandangan bahawa embryo atau janin yang belum terbentuk atau belum lagi berada di dalam rahim wanita tidak sabit hukum ke atasnya atau tidak ada hukum ke atasnya. Beliau menjelaskan :

"فلم يجعل الشرع للجنين قبل التخلق أي اعتبار، ولا بنى عليه أي حكم شرعي... وقد أبديت رأيي في هذا بإسهاب في مناقشات ندوة الإنجاب. وحتى في القرار الذي اتخذ في ندوة الإنجاب لم يجعل للبييضة الملقحة أية حرمة إلا بعد العلوق بجدار الرحم، أما قبل العلوق فلم يجعل القرار له أي حرمة."

Maksudnya : *"Syarak tidak menetapkan apa jua hukum ke atas janin yang belum terbentuk. Sesungguhnya saya telah menerangkan pandangan saya dengan terperinci dalam perbincangan forum mengenai kelahiran. Dalam forum tersebut keputusan telah dikeluarkan bahawa syariat Islam tidak menetapkan hukum pengharaman ke atas telur wanita yang sudah disenyawa kecuali selepas ianya berada di dalam rahim. Adapun sebelum berada di dalam rahim tidak sabit hukum ke atasnya."*

Pandangan sedemikian juga telah dikeluarkan oleh Institusi Fatwa (Darul Ifta') Arab Saudi di mana selagi belum ditiupkan roh pada janin tersebut, air mani dan telur tersebut dihukum hidup bersesuaian dengan keadaan masing-masing. Ia sebagai zat pembudidayaan atau pembenihan. Ia belum sampai ke tahap zat yang sempurna hidup. Berikut adalah teks fatwa Darul Ifta'tersebut:

لكل من الحيوان المنوي وبويضة المرأة حياة تناسبه إذا سلم من الآفات, تهيئ كلاً منهما بإذن الله وتقديره للاتحاد بالآخر , وعند ذلك يتكون الجنين إن شاء الله ذلك, ويكون حياً أيضاً حياة تناسبه حياة النمو والتنقل في الأطوار المعروفة , فإذا نفخ فيه الروح سرت فيه حياة أخرى بإذن الله اللطيف الخبير .

Yang bermaksud : "*Jika ditakdirkan air mani dan telur wanita tidak mati, kedua-duanya akan hidup sesuai dengan keadaan kedua-duanya (seperti yang diciptakan). Dengan izin Allah dan takdir-Nya kedua-duanya akan bersatu. Ketika itu akan terbentuklah janin dengan izin Allah. Dan janin itu hidup sesuai dengan perkembangannya dan peningkatannya mengikut tahap yang sudah ditetapkan. Apabila ditiup roh padanya akan berputik satu kehidupan dengan izin Allah yang Maha Lembut dan Maha Mengetahui*".

- **Kesimpulan**

Sehubungan dengan ini, Jawatankuasa Fatwa memfatwakan bahawa pandangan Jawatankuasa Penasihat Bioetika untuk menggunakan sel induk daripada embryo yang berusia tidak lebih daripada 14 hari, bagi tujuan penyelidikan untuk kebaikan manusia adalah dibenarkan dari segi syarak selagi ianya tidak disalahgunakan sama ada untuk tujuan pengklonan manusia, atau mencampur-adukkan nasab keturunan, atau pun yang boleh menyebabkan penghinaan atas kemuliaan manusia.

MAJLIS UGAMA ISLAM SINGAPURA
FATWA COMMITTEE SPECIAL MEETING
THURSDAY, 22nd November 2001

INTRODUCTION

The Bioethics Advisory Committee (BAC) is of the view that it accepts the use of embryos created from in-vitro fertilisation, which are less than 14 days old, for the purpose of serious research involving stem cells for the benefit of mankind.

Based on scientific research, human embryos, which are less than 14 days old, have no pain or sentience since only at the 14th day does a primitive streak appear and develop into the nervous system.

The *Fatwa* (Legal) Committee was requested to give a *fatwa* on this issue.

Prior to this, Muis had organised a talk on 8 Sep 2001 on Stem Cells and Genome, which was delivered by Assoc Prof Tusqa Too Heng Poon. The talk was attended by the Muis Council and the *Fatwa* Committee.

ISLAMIC LEGAL GUIDELINES

Based on the explanation and research on the issue, the *Fatwa* Committee is of the view that Islam welcomes academic research on human genome, genetic engineering and other related fields. However, such research must be utilised for the benefit of mankind in areas like the treatment of illnesses. The research has to be within the boundaries of principles in Islamic Jurisprudence, which include :

a) **There should not be any harm and nothing should be done to cause harm**

The principle means :-

- Do not cause harm to one's self and to others.
- Do not do something that will benefit one's self but will harm or cause difficulty to others.

b) **Harm should be avoided.**

The principle means :-

- Harm, which is sure to occur, should be avoided whether before or after it occurs.

POSITION OF EMBRYO IN ISLAMIC LAW

What is Islam's view on the fertilisation of an embryo within or outside the womb ?

The *Fatwa* Committee is of the view that Islam does not place any judgement on an embryo, which is not fully formed. An embryo is only considered as a human life after it is 4 months old as in Islam, it is believed that a soul is introduced into the embryo when it is 4 months old. This is the view of most jurists based on the *hadith* (Tradition) narrated by Abdullah bin Mas'ud which means :

"Verily the creation of each one of you is brought together in his mother's belly for forty days in the form of seed, then he is a clot of blood for a like period, then a morsel of flesh for a like period, then there is sent to him the angel who blows the breath of life into him and who is commanded about four matters: to write down his means of livelihood, his life span, his actions, and whether happy or unhappy..."

Related by Bukhari and Muslim.

Thus, an embryo below 4 months whether within or outside the womb, is considered as a living thing undergoing the growth process. However, it is not yet considered as the beginning of human life with the existence of a soul.

Past and present jurists have given a similar view. Among them include Dr Muhammad Sulaiman Al-Asyqar who is of the view that an embryo which is not formed or is not in a woman's womb, will not be placed any judgement on it. He explained :

"Islamic law does place any form of judgement on an embryo which is not formed. Verily, I have explained in detail my opinion during my forum discussion on birth. In that forum, decision had been made that Islamic law does not place any judgement on a woman's fertlised egg except after it is in the womb. There is no judgement on it before it is in the womb."

A similar opinion was also given by the Fatwa Institution of Darul Ifta', Saudi Arabia where, for as long as there is no soul in an embryo, the sperm and the egg are judged to be living things adapting to their specific conditions. They are considered as components of the fertilization process. The have not reached the stage of a complete human being. The following is the text from the fatwa of Darul Ifta' which means :

"If it is destined that the sperm and a woman's egg do not die, both will live adapting their respective conditions as created. With Allah's will and predestination, both will fuse. At that point, an embryo will be formed. The embryo will live according to its own growth and development following the

defined stages. When a soul is introduced, a human life will be created based on the will of Allah, who is the Subtle one and the All-Knowing".

CONCLUSION

In relation to this, the Fatwa Committee rules that the opinion of the Bioethics Advisory Committee to use stem cells from embryos below 14 days old for the purpose of research, which will benefit mankind, is allowed in Islam. This is with the condition that it is not misused for the purpose of human reproductive cloning, which would result in contamination of progeny and the loss of human dignity.

C. PROFESSIONAL GROUPS

1. Law Reform Committee, Singapore Academy of Law
2. The Law Society of Singapore
3. Singapore Hospice Council
4. Singapore Medical Association
5. Singapore Medical Council
6. Singapore Nurses Association
7. Singapore Nursing Board

S I N G A P O R E A C A D E M Y O F L A W

30 November, 2001

Professor Lim Pin
Chairman
Bioethics Advisory Committee
250 North Bridge Road
#15-01/02 Raffles City Tower
Singapore 179 101

Dear Prof Lim

Feedback Regarding Human Stem Cell Research in Singapore

Thank you for your letter dated 8 November 2001 and the enclosures.

2. The Law Reform Committee specially met to consider the consultation paper of the Human Stem Cell Research Subcommittee ('HSR'). In considering the paper, a couple of the members have also carried out some research on the matters raised, and provided the Committee with some helpful insights. We set out below our views on the various matters raised in the consultation paper.

Use of human embryos of less than 14 days old

3. At page 4 of the consultation paper, the HSR stated that human embryos of less than 14 days have no pain or sentience. We have two observations on this. First, this cut-off age of 14 days was presumably derived from research carried out many years ago, and was adopted in the United Kingdom for the purpose of certain legislation. We were given to understand that some researchers in the 1970s referred to embryos of less than 14 days as "pre-embryos", but that the term has since been discarded. It seems to us that closer investigation and research should be carried out now to determine the safest cut-off period. In this connection, we should point out that President George W Bush has authorised federal funding in the United States for embryonic stem cell lines cultivated from the inner cell mass of a *week-old* embryo (White House Statement, August 9, 2001). With the progress made in scientific and medical research, it is probably timely that the 14-day cut-off period should now be reviewed.

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4. Secondly, as we understand it, the 14-day cut-off period is adopted, presumably because an embryo in its first 14 days does not have any pain or sentience, its nervous system not having been developed. If our understanding is correct, some members question whether this is an appropriate way of determining the cut-off period. It might be argued that the question whether or not it is proper to do research on an embryo less than 14 days old should not be determined on the basis that the embryo does not feel any pain, just as the law does not require that a victim must feel pain before the crime or tort of assault is made out: the experience of pain is not an element which is required to be satisfied. To the extent that the 14-day cut-off period is based on the embryo's failure to feel pain, it is potentially inconsistent with the law.

Class of ES cells to be permitted in research

5. We note that a distinction is made in other reports between various classes of ES cells. For example, the United States has approved federal funding for research using ES Cells from embryos remaining after the conclusion of infertility treatments, which are intended to be discarded, because they are unsuitable or no longer needed for treatment. This is not the position with ES Cells derived from research embryos (created through IVF with gametes provided solely for research purposes); and ES Cells from embryos made using somatic cell nuclear transfer in oocytes (as this has the potential of creating a human embryo).

Ensuring independent donor consent

6. We note that in Singapore human embryos of less than 14 days, which are created through in-vitro (or in-vivo) fertilisation techniques but not used in assisted reproduction treatments, can be used for research, subject to observance of certain stringent guidelines. We understand that one of the requirements of such guidelines is that consent must be obtained from the donors of the gametes. In this respect, BAC is urged to consider seeking ***informed*** consent from donors, especially the consent from the gestational mothers, free from any inappropriate influences and without any financial or other inducements.

Consent at enrolment and at research process

7. Turning to international practice, we think that consent should be obtained not only at the stage when the in-vitro or in-vivo fertilisation process is to be performed, but also at the stage when the embryos would be used for research purposes. It is not difficult to envisage that consent would be readily given at the beginning prior to the in-vitro or in-vivo fertilisation process; however, subsequent experience may alter the position. As we see it, a material factor may well be the success or otherwise of the fertilisation process. Our view is that separate consent should be obtained from the donors, particularly the gestational mother, after the success or failure of fertilisation process, once it is determined that the "unwanted" embryos will be used for research.

Disclosure by Researchers

8. We would highlight that the United States Bioethics Advisory Committee recommended that researchers should fully reveal to the donors the potential use for research purposes of the embryos which would otherwise be discarded, by, among other things, the following:

- disclosing that the ES Cell research is not intended to provide medical benefit to embryo donors;
- ensuring that consent or refusal will not affect the quality of future care to prospective donors;
- describing the general area of research to be carried out;
- disclosing the potential commercial benefits, if known;
- affirming that the embryos used in research will not be transferred to any woman's uterus; and
- confirming that the research will involve the destruction of the uterus.

Legal Process

9. If research on the broad terms set out in the consultation paper is to be permitted, the process should be strictly regulated by legislation. As such research involves human life or potential human life (depending on which perspective is adopted), a breach of the conditions under which it can be performed should be criminalised and be made punishable by an appropriate penalty. Some guidance may be taken from the United Kingdom's latest Human Reproductive Cloning Bill passed by the House of Lords and sent down to the House of Commons on 26 November 2001.

Protections to extend across private and public sectors

10. Any regulations recommended should apply to both publicly-funded and privately-financed research projects in Singapore. We note that the 'oversight system' in the United States has historically resulted in ethically indefensible differences between protection given to participants in federally sponsored research and those outside the jurisdiction of the Food and Drug Administration's jurisdiction.

11. I hope our comments would be some assistance to BAC.

Yours sincerely

L P Thean

L P Thean
Chairman
Law Reform Committee

THE LAW SOCIETY OF SINGAPORE

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18 December 2001

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F R O M T H E P R E S I D E N T

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Chairman
The Bioethics Advisory Committee
250 North Bridge Road
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Singapore 179101

Dear Prof. Lim Pin

Request for Feedback Regarding Human Stem Cell Research in Singapore

I refer to your request for feedback from the Law Society regarding human stem cell research in Singapore. Your Committee has sought the views of various interest groups, and I am confident that moral and ethical issues have been extensively explored and discussed; our feedback herein will thus not dwell on such issues.

I shall deal with the legal position in Singapore – as it now stands.

Stem cell lines are evidently protectable under Patent Law. Inventions relating to this matter are capable of patent protection in USA, and numerous other countries. There appears to be no impediment to its registration as patents in Singapore as long as the steps taken are new, inventive and industrially applicable; such matters are not excluded under section 13(3) of the Patents Act 1994.

However, numerous issues do arise. One issue concerns the ownership of the cells developed from the stem cell lines. Another issue is the ownership of the intellectual property rights for the medical discoveries resulting from research using those stem cells.

Another issue is consent. The necessity for informed consent from the biological parent should be enshrined for stem cell research in the same way as consent for clinical trials, which is set out exhaustively in section 14 of the Medicines Act, Cap 176. The present law on stem cells are inadequate. As the law now stands, embryos removed during medical procedure, may be used without the knowledge or consent of the woman undergoing the procedure. Also, the Termination of Pregnancy Act, Cap 234, does not contain any guidelines on the treatment of aborted foetuses.

The informed consent should therefore be sufficiently detailed and ought to include a statement that the embryos or foetal tissues may be used to derive human pluripotent stem cells for research that may include transplantation research, that the derived cells may be kept for many years, that the research is not intended to provide direct medical benefit to the donor, and that the donated embryos will not be transferred to a woman's uterus and will not survive the stem cell derivation process. It must also state the possibility that the results of the research may have commercial potential, and that the donor will not receive any benefits from any such future commercial development.

There is need for guidelines to govern research using pluripotent stem cells. I would suggest your Committee study and adopt the US National Institute of Health (NIH) Guidelines on such research. However, unlike USA, where the Guidelines applies to NIH funded research, I request the Committee to apply the Guidelines to all research on stem cell lines conducted in Singapore. I seek to suggest, too, that the Committee studies the Human Fertilisation and Embryology Act 1990 when considering and deciding on guidelines for Singapore.

The solutions to these issues should be carefully deliberated before a decision is taken to enshrine it in legislation, and the accompanying Guidelines or Rules. The Law Society will be pleased to participate in further discussions.

Yours

Palakrishnan, SC
President

cc Council

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24 December 2001

F R O M T H E P R E S I D E N T

Prof Lim Pin
Chairman
Bioethics Advisory Committee
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Attn: Ms Lauren Noto

Dear Prof Lim

STEM CELL RESEARCH

I have your letter of the 18th instant.

Aside from the proposed Meeting in January 2002, I enclose a copy of a Discussion Paper produced by the Law Institute of Victoria, Australia, for your information and retention.

Yours sincerely

Palakrishnan, SC
President

Enc

The Ownership of Genetic Information and Genetic Material

March, 2000

Law Institute Victoria

Discussion Paper

Contents

Part A - The Ownership of Genetic Information

1. Introduction

Biotechnology is a burgeoning industry. In 1998 the total revenue earned by Australia's 120 core biotechnology companies exceeded 965 million dollars and employed about 4,000 people.[1] It is predicted that this industry will continue to be a driving force in economic and employment growth over the next thirty years, based on Australia's strong fundamentals in research science. Patent grants are important as they encourage financial investment in this area. Genetic information and material are patentable under Australian law and thousands of biological patent applications have already been lodged with the Australian Patent Office. Some are for DNA, genes, genetic sequences and the like. Others are for whole plants and animals.

1.1 Potential uses of biological inventions

Many biological inventions have significant uses in medicine and science, agriculture, the food industry, and environmental uses.

Medicine and science: Diagnostic tests have been developed to detect genetic and other conditions in humans and animals. Insulin, antibiotics, vaccines and new drugs manufactured using genetic manipulation techniques are already being used in human and animal health care. Human diseases that may be treated in future include cancer and multiple sclerosis. An important aspect of the development of new pharmaceuticals is that they can be extracted from the milk of animals genetically manipulated to produce biological substances. This makes the products cheaper to manufacture and also safer. In the future, specially bred animals may become donors of organs and tissue for human patients. Another innovation of particular promise is gene therapy. The ability to replace defective genes with functional genes may one day eliminate genetic disease.

Agriculture: Genetically manipulated crops and animals are being produced that grow faster and are more productive (eg rice with vitamins added for third countries; animals with a higher meat to fat ratio). Crops that are more resistant to disease and pests are already coming onto the market in Australia. Others that are resistant to particular herbicides and pesticides allow a larger quantity of those products to be used early in the growing season to kill weeds and pests, reducing the need for more frequent applications and reducing the overall use of herbicides and pesticides.

Food industry: Fungi, such as yeast for bread making and enzymes used in fermentation processes, have been patented and used in the food industry for many years. More recent advances in biotechnology show promise in generating new food preservatives. New plant varieties developed from traditional breeding methods have also been patented.

Environmental uses: Pollution control, toxic waste management, hydrocarbon breakdown ("oil eating bacteria") have been suggested as potential environmental uses of genetically manipulated organisms.

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[1] Ernst & Young, *Australian Biotechnology Report* (October 1999), 11.

1.2 This paper

This part of the paper analyses the Australian law and experience to date concerning biological patents, as well as the law in the United States and Europe. It then sets out arguments for and against patents on genes and genetic sequences.[2] It outlines a number of proposals in Australia and other countries to change the law together with options for regulating biological patents in Australia.

2. Current Law in Australia

2.1 What is patentable?

As of March 1997, the Patent Office had received some 8,100 applications for gene or gene sequences and granted some 2,100 patents.[3] They include patents on micro-organisms such as bacteria, fungi and viruses; DNA, genes and chromosomes; synthetic genes or DNA sequences and the DNA coding for a gene; plants; and non-human animals.[4] DNA or genes in the human body are not patentable but "a DNA or gene sequence which has been separated from the human body and manufactured synthetically for reintroduction into the human body for therapeutic purposes is patentable".[5] "Products of such living patented matter, eg food supplements, drugs and processes for synthesising the material or making the products" are also patentable.[6] So are other applications of patentable inventions – probes for a particular gene; higher plants/animals carrying the gene; and methods for using a gene or genetic technology.[7] "Human beings, and the biological processes for their generation" are not patentable as they are specifically excluded under section (s) 18(2) of the Patents Act 1900 (Cth).

2.2 Patents Act 1990 (Cth)

In order to be patentable, a biological invention must meet the requirements of section 18 of the *Patents Act* 1990 (Cth). Section 18 provides:

> "18(1) Subject to subsection (2), a patentable invention is an invention that, so far as claimed in any claim:
>
> (a) is a manner of manufacture within the meaning of s 6 of the *Statute of Monopolies*; and
>
> (b) when compared with the prior art base as it existed before the priority date of that claim:
>
> (i) is novel; and

---

[2] Although other forms of intellectual property may be relevant to genetic information and material (eg plant variety legislation, trade marks, copyright), patents are by far the most important and are thus the focus of this paper.

[3] Senate Question on Notice 449, 24 March 1997. See also C Lawson, 'Patenting Genes and Gene Sequences in Australia' 1998 (5) *Journal of Law and Medicine* 364, 366.

[4] IP Australia Pamphlet, *Australian Patents for Microorganisms, Cell Lines, Hybridomas, Related Biological Materials and Their Use, Genetically Manipulated Organisms* (Nov, 1998) 1.

[5] Ibid.

[6] Ibid.

[7] Ibid.

(ii) involves an inventive step; and

(c) is useful; and

(d) was not secretly used in the patent area before the priority date of that claim....."

Subsection (2) provides:

"(2) Human beings, and the biological processes for their generation, are not patentable inventions".

There are thus four main requirements that must be satisfied for a patent to be granted. (i) It must be a manner of manufacture. (ii) It must be novel and involve an inventive step. (iii) It must be useful. (iv) It must not have been secretly used prior to the application of the patent. Although there is an extensive body of case law on the elements of patentability,[8] the following discussion focuses principally on these criteria.

2.2.1 It must be a manner of manufacture

The requirement that an invention must be a "manner of manufacture" means that it must be possible to reproduce the product or process for which the patent is sought by following the specifications in the patent application. (Under the Budapest Treaty, to which Australia acceded in July 1987, this requirement can be also met by depositing a sample of a biological substance instead of a description of how to produce it. However, the fact that the sample is then available to researchers to use directly is an obvious disincentive to follow this procedure, which is optional.) The product must also be useful, have some material advantage, have some economic advantage and have an industrial application - an innovative idea that provides a practical solution to a technical problem.[9] It may be a new product, a new method of producing an existing product, or a new use for an existing product.

Furthermore, an invention is not patentable subject matter if it is a mere discovery. The observation of certain physical properties of an existing substance, or the finding of a previously unknown but naturally occurring substance, is not something that is patentable.[10] For instance the laws of physics are not patentable subject matter. However, the distinction between a discovery and an invention is not precise, as was noted by the High Court of Australia in *National Research Development Corporation v Commissioner of Patents*.[11] In that case, the court insisted that the whole process must be looked at and one inventive step in the process might justify a patent.[12] Therefore although the identification of a naturally occurring gene sequence may be a discovery,

[8] See,eg: S Ricketson, *Intellectual Property Cases Materials and Commentary* (Butterworths, 1994) chs 13 and 14.

[9] IP Australia Pamphlet, above n 4, 2.

[10] J McKeough and A Stewart, *Intellectual Property in Australia* (2nd ed, 1997) 290.

[11] (1959) 102 CLR 252, 264.

[12] Ibid.

the isolation and characterisation of the gene and utilisation of that knowledge to make a synthetic gene and gene products, will be patentable inventions.[13]

The distinction between discoveries and inventions is also illustrated by another Australian case, *Kiren-Amhgen Inc v Board of Regents of the University of Washington.*[14] That case involved a patent application for the purified or isolated DNA sequence encoding the human protein erythropoietin. The Deputy Commissioner of Patents stated that a claim directed to a naturally occurring DNA sequence would be claiming no more than a discovery per se and not be a manner of manufacture.[15] However, because the claim specified a purified and isolated DNA sequence, the claim related to "an artificially created state of affairs", and thus was a manner of manufacture.[16]

2.2.2 It must be novel

The assessment of novelty basically requires an investigation to establish whether the alleged invention has been anticipated, judged at the time of the patent application. Anticipation principally occurs through prior publication or prior use.[17] The Australian Patent Office has specified that the requirement of novelty with respect to gene sequences and related biological materials is satisfied if the subject matter is new in the sense of not previously being available. That is, a patent cannot be granted for materials in their naturally occurring state or for materials that have previously been made publicly available.[18]

2.2.3 It must be inventive

In addition to being novel, the invention must involve a degree of inventiveness. To establish an inventive step one must ask the question: Was it, for practical purposes, obvious to a person skilled in the particular art, armed with all the common general knowledge of his or her art, that he or she could do what the patent proposes?[19] In most instances this requirement is easily met as there need be only a "scintilla of invention".[20] Academic commentators in Australia have argued that the cloning and sequencing of a gene is unlikely to amount to an inventive step. Once information about an amino acid sequence is known, then to a person skilled in the art of molecular biology, with common general knowledge, the cloning and sequencing of a gene is the obvious next step.[21] However the Patent Office does not seem to hold this opinion and the

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[13] D Nicol, 'Should Human Genes be Patentable Inventions under Australian Patent Law' (1996) 3 *Journal of Law and Medicine* 231, 238, citing the Australian Patent Office, *Manual of Practice and Procedures* ss 8.1.15.2(c), 8.1.15.3.
[14] (1995) 33 IPR 557.
[15] Ibid 569.
[16] Ibid.
[17] *Griffin v Isaacs* (1938) 12 AOJP 739. See also McKeough, above n 9, 297.
[18] IP Australia Pamphlet, above n 4, 2.
[19] *Patents Act* 1900 (Cth) s 7(2).
[20] *Samuel Parks & Co Ltd v Cocker Bros Ltd* (1929) 46 RPC 241, 248.
[21] See comment by C Lawson, 'Patenting Genetic Materials: Old Rules May be Restricting the Exploitation of a New Technology' 1999 (6) *Journal of Law and Medicine* 373, 379.

requirement of inventiveness has not proved an obstacle to the patenting of genetic sequences in Australia.[22]

2.2.4 It must be useful

The requirement that the invention must be useful means that there must be an actual use for the invention rather than speculation as to future uses;[23] and the Australian Patent Office has specified that the use must be fully described. For example, it may be used to treat human diseases such as cancer or multiple sclerosis. However, a genetic sequence on its own which lacks some function, component or application is not patentable for lack of utility.

2.2.5 Human beings are not patentable

Section 18(2) of the *Patents Act* (Cth) provides that human beings, and the biological processes for their generation, are not patentable inventions. The Patent Office has stated that the only limitation that this exclusion creates in the area of genetic research is that DNA or genes in the human body are not patentable as such.[24]

3. Law in other countries

3.1 United States

Since 1980, it has been well settled law in the United States that nucleic acid sequences, isolated genes, isolated proteins and organisms are patentable.[25] In that year, the United States Supreme Court held that a genetically engineered bacterium capable of breaking down oil spills was patentable (*Diamond v Chakrabarty*[26]). Since then, the United States Patent Office has granted some 12,000 patents on inventions related to DNA sequences.[27] Patents have also been granted for plants and animals. An example of the latter is the Harvard oncomouse, genetically manipulated to develop tumours and so useful in cancer research on diagnosing and treating tumours.

Patent law in the United States requires three technical requirements; novelty, utility and non-obviousness.[28] Novelty involves a judgment whether the invention is truly something new and original.[29] Utility requires that the invention has some articulated use.[30] Non-obviousness requires a hypothetical judgment by a person with ordinary skill

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[22] This is illustrated by the cases of *Hoffmann-La Roche AG v Bresagen Ltd* (1997) 40 IPR 53, and *Kiren-Amhgen Incorporated v Board of Regents of University of Washington* (1995) 33 IPR 557.
[23] IP Australia Pamphlet, above n 4, 2.
[24] Nicol, above n 13, 241.
[25] Committee no 1001, Chaired by H L Baker, Section of Intellectual Property Law, Annual Report 1995-96, American Bar Association, Chicago, Illinois.
[26] 447 US 303 (1980)
[27] As of October 1999 - determined using IBM Intellectual Property Network database.
[28] See 35 USC 100-12
[29] 35 USC 101-102. With respect to genetic sequences it was held in the case of *Amgen, Inc v Chughai Pharmaceutical Co Ltd* 927 F2d 1200, 1203. that the requirement of novelty is satisfied if the sequences are "purified and isolated".
[30] 35 USC 101.

in a particular field to determine whether the invention is more than an obvious progression in the field.[31]

The requirement of utility in respect of gene sequences has caused considerable debate in the United States. The grounds required to establish utility were discussed in the case of *Brenner v Manson*.[32] The Supreme Court said that "unless and until a process is refined and developed to the point of a substantial utility - where a specific benefit exists in currently available form - there is insufficient justification for permitting an applicant to engross what may prove to be a broad field."[33] The court expressly recognised that an invention "which either has no known use or is useful only in the sense that it may be an object of scientific research"[34] is not patentable. It was because of this requirement that an application by the United States National Institutes of Health (NIH) in 1991 for a patent on some 2,000 gene sequences (ESTs[35]) failed. The function of the genes was unknown, and mere use of the sequences as probes was unacceptable. There was not the requisite degree of specific benefit - they were mere research tools. However in 1995 the United States Patent Office issued guidelines on assessing utility which are far more generous. According to these guidelines one need only establish a "credible utility". "Credible utility" is defined as "whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided".[36] Academic commentators have argued that this broader test makes a utility rejection highly unlikely.[37] It has been suggested that they are of such breadth that the use of ESTs as probes satisfies the utility requirement, and are therefore patentable.[38] This has been confirmed by the United States Patent Office which has stated that ESTs, in principle, are patentable.[39] This has caused considerable concern among researchers - that their basic tools might be subject to patent rights.

With respect to obviousness, the United States Court of Appeals has found that genes and gene sequences for proteins of known function are patentable (*Re Duel*[40] and *Re Bell*[41]). This is because the sequence would not have been known without cloning and sequencing, which is sufficient for it to be non obvious.[42] In both cases the court accepted that degeneracy in the genetic code meant that a number of different nucleotide sequences might code for a specific protein, and therefore the nucleotide sequence

[31] 35 USC 103.
[32] 383 US 519 (1966)
[33] Ibid 534-535.
[34] Ibid 535.
[35] Expression Sequence Tags, are segments of DNA, of unknown function which are routinely used by researchers in gene discovery.
[36] 'PTO Examination guidelines on Utility Requirements', 50 *Patent, Trademark and Copyright Journal* 295, 303.
[37] A Kight, 'Pregnant with Ambiguity: Credibility and the PTO Utility Guidelines in Light of *Brenner*' (1998) 73 *Indiana Law Journal* 997, 1015.
[38] Ibid 1019.
[39] C O'Brien, 'US Decision Will Not Limit Gene Patents' (1997) 385 *Nature* 755. See also S Bent and P Booth, 'Genomics Races Raises Ownership Boundary Issue' Foley and Lardner <http://www.foleylardner.com/PG/IP_BIOT/genomics.html>
[40] 51 F 3d 1552, 1558 (1995)
[41] 999 F 2d 781, 784 (1993)
[42] The court in coming to this conclusion focused on the non-obviousness of the sequence itself, as opposed to the nonobviousness of the method of sequencing.

claimed was not obvious.[43] A result of these decisions is that prior disclosure of an amino acid sequence does not necessarily render obvious the DNA molecules that encode the protein, further widening the scope for patenting DNA sequences. More recently the legislature in the United States passed the *Biotechnological Process Patent Act* 1995, which strips biotechnological processes of the presumption of unobviousness. As a result, an applicant applying for a patent over a biotechnological process has the option of waiving the requirement that the process itself be found unobvious.[44]

3.2 Europe

Patent law in Europe is governed largely by the European Patent Convention. Article 52 provides that for an invention to be patentable it must be an invention; novel; present an inventive activity; and have an industrial application. As in the United States and Australia, there was initially some dispute as to whether a gene or genetic sequence met these criteria. There were also concerns about the morality of patenting larger organisms.

In relation to genes and genetic sequences, the European Parliament and European Commission passed a directive on the legal protection of biotechnological inventions in order to make it clear that these could be patented. The preamble to the directive recognises that biotechnological inventions are playing an increasingly important role in a broad range of industries.[45] Research and development in the field of genetic engineering is a high risk investment and therefore requires adequate legal protection.[46] Developing biotechnology should be encouraged by the patent system as it is important in combating disease and hunger.[47] The human body and its elements are unpatenable in their natural state because patent law should respect the fundamental principles safeguarding the dignity and integrity of a person.[48] Yet the directive clearly makes provision for the patenting of human DNA sequences. Article 3 states that inventions that are new, involve an inventive step and are susceptible of industrial application will be patentable even if they concern a product consisting of biological material. Article 5 provides that an element isolated from the human body, including the sequence of a gene, may constitute a patentable invention.[49] However, a mere DNA sequence without indication of a function is not a patentable invention.[50] The two key requirements are an isolated gene sequence and knowledge of the gene's function.

An additional limiting factor is that, in Europe, inventions must not be contrary to ordre public or morality. Article 6 provides that such inventions are unpatentable.[51] The

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[43] *Re Duel* 51 F 3d 1552, 1558 (1995); *Re Bell* 999 F 2d 781, 784 (1993). See also Lawson, above n 21, 380.

[44] S Maeblus, 'Biotechnological Process Patent Act: Legislative Relief for Process Claims' Foley and Lardner <http://www.foleylardner.com/PG/IP_BIOT/pate20_biot.html>

[45] *Directive of the European Parliament and of the Council on the Legal Protection of Biotechnological Inventions*, 6 July 1998, 98/44/EC, recital 1.

[46] Ibid, recital 2.

[47] Ibid, recital 11.

[48] Ibid, recital 16.

[49] Ibid, article 5(2).

[50] Ibid, recital 23 and article 5(1).

[51] Ibid, article 6(1).

directive specifies that the cloning of human beings and the use of human embryos for industrial or commercial purposes fall within this category.[52]

4. Arguments in favour of biological patents

Sections 4, 5 and 6 below set out the arguments for and against biological patents and then evaluate those arguments.

4.1. Patents encourage research and development

Patents provide an incentive for research and development. They encourage investment in biotechnology, a risky and financially unrewarding endeavour. Without this investment, new drugs and treatment will not be developed. Denying patent protection would lead to increased secrecy and delay research and the release of new drugs, to the detriment of the community.[53]

4.2 Patents encourage dissemination of information

Patents inform the public about the results of scientific research because a patent will not be granted without full disclosure. Other researchers will learn about the invention and not undertake unnecessary duplication of research.[54]

5. Arguments against biological patents

5.1 Religious objections: usurping God's province

Humans and animals are creations of God, not humans, and as such should not be patented as human inventions.[55] Patenting of genomic sequences "represents the usurpation of the ownership rights of the sovereign of the universe".[56] A coalition representing more than eighty faiths and denominations, including Catholics, Evangelicals, Protestants, Jews, Muslims and Buddhists have declared their opposition to the patenting of genetically engineered animals, human genes, cells and organs.[57]

5.2 Genetic information is commonly owned

The human genome is a common, universal possession, representative of humankind's collective heritage.[58] The genome is thus not a proper subject matter for intellectual

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[52] Ibid, article 6(2).
[53] See comments in G Poste, 'The case for genomic Patenting' 1995 (378) *Nature* 536.
[54] Nicol, above n 13, 232.
[55] Foundation for Economic trends and General Board of Church and Society of the United Methodist Church, statement issued at press conference, 18th May 1995, Washington DC. See also, K Woodward, 'Thou Shalt Not Patent!' (1995) May 29 *Newsweek* 68.
[56] R Stone, 'Religious Leaders Oppose Patenting Genes and Animals' (1995) 268 *Science* 1126.
[57] Ibid.
[58] Note the comments made by H Curien, 'The Human genome Project and Patents' (1991) 254 *Science* 1710.

property rights.[59] Everyone is entitled to share any economic benefit from genetic research. Also, biological patents would inevitably benefit wealthy countries and corporations more than poor ones, when all humans should enjoy such benefits.[60]

5.3 Biocolonialism

Allowing wealthy countries to patent genetic material from poorer countries encourages biocolonialism (ie the exploitation of the biological resources of other countries). Examples include a patent obtained by the United States National Institutes of Health for an unusual variant of HIV obtained from the Hagahai people of Papua New Guinea; and a genetically engineered variant of South East Asian Basmati rice which may put small Asian farmers out of business.[61] Australia as a mega diverse nation should protect its genetic diversity by banning the patenting of DNA sequences.

5.4 Collective and individual privacy

Genes are the building blocks of human life. They are part of everyone's body, as well as their intellectual and emotional constitution. Allowing genes to be patented by a third party without a person's consent infringes that person's right to privacy;[62] or the privacy rights of the group or race to which the person belongs.

5.5 Patenting genes and genetic sequences increases costs for other researchers and the community

Patents on genes and genetic sequences impose an extra cost on researchers who want to use them in more extensive research. For example, the pharmaceutical giant Merck has argued that restricting access to basic structural and descriptive information about the genome through patents will prevent the human genome being extensively exploited.[63]

Multiple patents also increase the cost of genetic testing. If the research was initially government-sponsored, the public pays twice – first, for the project that ultimately results in a patent and later, for using the patented product.

5.6 Patents may delay research and product development

Some commentators have questioned the assumption that companies will not undertake research without the incentive of patent protection. Indeed, if a competitor holds a patent that covers part of the area in question, that may be a disincentive to others to

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[59] B Looney, 'Should Genes be Patented? The Gene Patenting Controversy: Legal, Ethical, and Policy Foundations of an International Agreement' 1994 (26) *Law and Policy in International Business* 231, 234. Cf Universal Declaration on Human Rights Article 27: each person in the world should share in the benefits of scientific advancement and particularly in the "moral and material interests resulting from any scientific, literary or artistic production of which he is an author".

[60] Looney, above n 59, 240.

[61] D Wertz, 'Controversial Attempts at Patenting' 1999 3(2) *The Gene Letter* <http://www.geneletter.org>

[62] Looney, above n 59, 238.

[63] D Dickson, 'Open Access to Sequence Data will Boost Hunt for Breast Cancer Gene' (1995) 378 *Nature* 425. One should add after exploited: "until after the patent period".

undertake research. An example cited by Charles Lawson is the case of *Murex Diagnostics Australia Pty Ltd v Chiron Corporation and Ortho Diagnostic Systems Inc.*[64] Lawson argues that, if the patent claimed by Chiron on Hepatitis C strain 1a had been upheld, that would have precluded Murex offering a more extensive test for other Hepatitis C strains not covered by the Chiron test. Australian blood suppliers would then have been able to test only for Hepatitis C strain 1a and not for the more prevalent strains 2, 3 and 5, causing increased anguish to those affected and increased costs to the community.[65] The conflicting parties might reach agreement through cross-licensing but the cost of that negotiation and the reduction in profitability of its potential product are still a disincentive to pursue the research.[66]

6. Evaluation of arguments concerning biological patents

It seems clear that patents generally do encourage research, disclosure of information and the development of new products. Those who say that patents promote secrecy often do not understand the requirement of patent law that the details of an invention must be revealed, together with instructions for reproducing it, before the patent will be granted. Also, if the patent holder refuses to allow others to use the patented invention, the Patents Act 1900 (Cth) contains provisions allowing a court application for a compulsory licence to be granted to someone who wants to use the invention. As a general principle, patents do not restrict or delay research.

They do, however, add to the cost of research and may affect the type of research that is undertaken. This is especially so with patents on the basis "tools" of research in biotechnology, such as genes and genetic sequences. Although it seems fair to reward the finder of a new gene or genetic sequence, it must be remembered that one person's product is another person's tool[67] and that that person will have to pay each time the tool is used. Being required to pay for the basic material for biological research is a disincentive, especially in the straitened circumstances facing universities and other research centres today. And naturally, researchers funded by the private sector will use biological tools that their sponsor has already developed and patented – because they do not have to pay for access to it – and also, because they may develop further profitable uses for it. Yet, those tools may not be the most appropriate for the task.

These factors have influenced opponents of biological patents to argue that patents on at least genes and sequences should not be permitted, even if patents are allowed on whole

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[64] unreported, Federal Court, (NG380/1996).

[65] C Lawson, "Patenting Genes and Gene Sequences in Australia" (1998) 5 *Journal of Law and Medicine* 363, 364-5. Lawson argues that the grant of patents of genes and gene sequences "fails to take account of s 6 of the Statute of Monopolies. That section requires that the invention should 'be not contrary to the law or mischievous to the state by raising process of commodities at home, or hurt trade, or generally inconvenient'": ibid at 364. He advocates legislation (*semble* to prevent or restrict patents and genetic sequences) first because the powers of the Patent Office are limited in looking at the broader implications of a patent (p 365-6); and judges have declined to consider policy arguments concerning patents as those are a matter for Parliament (p 370).

[66] Lawson, ibid at 369, citing *Kirin-Ambgen Inc v Board of Regents of University of Washington and Genetics Institute Inc* [1995] 64 AIPO (19 Oct 1995).

[67] This was discussed at the First International Conference on DNA Sampling in Montreal, reported by Loane Skene and Donald Chalmers, (1997) 4 *Journal of Law and Medicine* 229-234.

organisms. However, the issue is not clear cut. Even if patents are granted, they are only for a limited period and the patented tool can still be used in research, though at a cost. More importantly, a patent holder can waive patent rights and that often occurs where there is a request from a university or private researcher who will not profit financially from using the invention. Finally, in future as it becomes easier and cheaper to isolate genes, more emphasis may be placed on their "utility" and fewer may be granted. Other technologies have gone through a similar stage with numerous patents, including "tools"; for example, in information technology.

In relation to the patenting of organisms, the objections to what some people see as the commodification of the basic elements of life – or the usurping of God's role – are met to some degree by the fact that a patent is not the same as ownership. With third world countries or collectivities, it is true that their biological material may be used in research, or even commercialised, but there are also potential benefits for those people from the research (new drugs and other medical treatments; genealogical knowledge; more productive agricultural animals and crops etc). Countries with strong economies gain greatest financial benefit in the early stages of a patent but later, patent-holders may choose not to register their patent in many countries or not to defend apparent breaches of the patent. It must be emphasised again that they do not own the product; they have an intellectual property interest in it for a limited period.

7. Recent Recommendations and Proposals for Change

7.1 Two Bills that would have prevented gene patents

Two Australian Bills that would have prevented gene patents were not pursued.

In 1990, Senator Coulter proposed an amendment to section 18 of the *Patents Bill* 1990 (Cth) (1990) that "A patentable invention should not include a gene or genes, whether derived from cells or chemically synthesised".[68] The amendment failed to win Senate support.

In 1996, Senator Stott-Despoja proposed the *Patents Amendment Bill* 1996 (Cth) (1996). It provided that naturally occurring genes, gene sequences and descriptions of the base sequence of naturally occurring genes do not possess the quality of novelty and inventiveness and should not be patentable.[69] The debate was adjourned, and the bill subsequently lapsed.

7.2 AMA concerns

The Australian Medical Association (AMA) said in its *Position Statement on Genetic Issues* (1988) that the holding of patents should not infringe the principle that the human genome is the common heritage of humanity and should not prevent an obstacle to the prevention, management and treatment of disease.[70]

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[68] Senate, *Hansard*, 17th September 1990, p 2478.
[69] *Patents Amendment Bill* 1996 (Cth) Schedule 1, 1. Senate, *Hansard*, 27th June, p2332.
[70] AMA 'Genetic Issues - 1998', Australian Medical Association, 1.

7.3 Later proposals in Australia and the UK would not prevent gene patents

There have been a number of policy recommendations that have supported the grant of biological patents, in some cases with limits. These are noted in paragraphs 7.3 and 7.4. The limits suggested are noted especially in paragraph 7.4.

7.3.1 ***Genetic Privacy and Non-Discrimination Bill 1998 (Cth).*** The most recent proposal relevant to patents of human biological material is the Genetic Privacy and Non-Discrimination Bill 1998 (Cth), introduced in the Australian Senate by Senator Stott Despoja. The scheme of the Bill would not prevent the patenting of human genetic material but samples could not be obtained or patents sought without the full consent of the person concerned. The Bill is based on the principle that people have dominion over their bodies and that they should therefore have sole right to decide who should have access to their genetic information and material. Under the Bill, DNA could not be collected, stored or analysed without the written authorisation of the person concerned after specified information and a specified notice of rights and assurances has been provided. The person would have the right to require that the sample be destroyed at any time and to share in the proceeds of any commercial exploitation of the tissue.

7.3.2 House of Representatives Standing Committee on Industry, Science and Technology, ***Genetic Manipulation: The Threat or the Glory*** **(1992).** This Committee concluded in 1992 that there is no justification for denying the biotechnology industry the opportunity to use the Patents Act to seek a reward for effort.[71] Denying the right to patent, allowed in other countries, would probably adversely affect the biotechnology industry in Australia.[72]

7.3.3 House of Commons Science and Technology Committee, ***Human Genetics: The Science and its Consequences*** **(1995).** The House of Commons Science and Technology Committee took a similar view in England in 1995. It said that patenting of genetic sequences should be permitted provided the application displays the requisite degree of novelty and utility.[73] Patent exclusion on the ground of morality should remain, given the increased importance of the concept of human dignity[74] but patents of DNA sequences do not fall within that exclusion.

7.4 Calls for limits on gene patents

However, some reports, while supporting biological patents, have called for limits. The need to obtain full consent from human donors has been noted above (para 7.2.1). Also, the English concern about morality (para 7.2.3). Two other reports suggest other limits.

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[71] House of Representative Standing Committee on Industry, Science and Technology, *Genetic Manipulation: The Threat or the Glory* (February 1992), 7.113.
[72] Ibid 7.112.
[73] House of Commons Science and Technology Committee, Third Report, *Human Genetics: The Science and its Consequences* (1995), xix, para 205.
[74] Ibid xvii, para 195.

7.4.1 Prime Minister's Science, Engineering and Innovation Council (PMSEIC), *Profiting from the Biotechnology Revolution* (1998).[75] In 1998, the PMSEIC stated that the international patent system should be changed to be far less supportive of monopolies in genetics.[76] In some cases, it said, broader than necessary patent protection had been given, particularly for naturally occurring genes.[77] However, limiting the coverage of a patent, compared with coverage in many other countries would probably adversely affect the biotechnology industry in Australia. An international initiative should therefore be encouraged to influence World Trade Organisation forums such as the Trade Related Intellectual Property agreement (TRIPS) to narrow the scope of patents for naturally occurring genes.

7.4.2 Advocates of a Human Genome Trust. A number of academics have proposed the creation of a world genome trust. Such a trust would oversee human genome research, holding gene sequences in trust for humanity. Its board would license researchers to protect rights prior to the development of patentable inventions.[78] It could check unethical development, alleviating some of the fear and mistrust associated with genetic research.[79] Advocates of the Human Genome Trust argue that it recognises the ethical reasons not to patent genes, but preserves the economic incentive of a patent system, finding a compromise between the competing ethical positions of the gene patenting controversy.[80]

8. Options for Legal Regulation in the Future

8.1 Continue to apply existing patent legislation

The first option is to continue to apply the existing principles of patent law. This will facilitate the exploitation of the emerging biotechnology industry. Investment will continue, encouraged by the monopoly protection of a patent. Although it is likely that genetic patents will be concentrated in a number of transnational companies and developed countries, the products will be available for everyone to use. Broad patent applications will probably be accepted under existing law and may limit the fullest exploitation of genetic material;[81] but the patents will eventually lapse, and the information and use of the invention will be freely available.

8.2 Ban the patenting of genes and genetic sequences

The second option is to allow biological patents to continue as at present but to ban or restrict patents on genes or genetic sequences. This would make genetic tools more readily available for researchers wanting to use them in other research. However, there

[75] Independent Working Group chaired by Chief Executive of the CSIRO Dr Malcolm McIntosh, '*Profiting From the Biotechnology Revolution*' Prime Minister's Science, Engineering and Innovation Council, (29th May 1998)
[76] Ibid 8.
[77] Ibid.
[78] Looney, above n 59, 268.
[79] Ibid, 270.
[80] Ibid, 272.
[81] Lawson, above n 21, 373.

would be less incentive for research to isolate and identify new genes and sequences. This would then have an adverse effect on scientific research in Australia. In addition, Australia may be in breach of international agreements, specifically the Trade Related Aspects of Intellectual Property Rights agreement. Article 27(1) of this agreement provides that "patents shall be available for any inventions, whether products or processes, in all fields of technology, provided that they are new, involve an inventive step and are capable of industrial application".

8.3 Lobby at an International level for more stringent patents

A third option for people concerned about biological patents is to lobby international trade organisations such as the World Trade Organisation and the World International Property Office to limit the scope of gene patents, while maintaining the existing patent framework. This would still maintain an economic incentive for research in biotechnology, while preventing broad monopolies, which may restrict future research.

8.4 Creation of a Human Genome Trust

Finally, people concerned about biological patents might support the concept of international projects such as a human genome trust. This might enable ethical concerns to be considered at a global level. However, this would require a major collaborative effort, especially by the leading developed countries. One is likely to encounter political tension, imbalances of power and bureaucratic waste.[82] It would raise difficult issues with existing patents on the human genome, and it fails to consider patents on gene sequences from other organisms.

9. Conclusion

Australia has much to gain from the emerging biotechnology industry that is already producing major financial returns in the United States and the United Kingdom, where biological patents are allowed, as they are in Australia. The Australian Patent Office has a clear policy for granting biological patents. Many have already been granted and there are many more applications awaiting consideration. Australia also has international treaty obligations that prevent the refusal of patent protection in Australia. A number of policy committees have considered whether biological patents should be restricted and have recommended that they should be allowed.

Although concerns have been expressed about biological patents, many of these are ill informed. They can often be met by explaining that patents apply only for a limited period, are not ownership and do not promote secrecy. However, some objections do need to be considered more closely, especially the effect of patenting genetic tools – genes and genetic sequences. The incentive to work on finding new genetic tools must be balanced against the increased cost to other researchers wanting to use those tools. This balance may be achieved by applying a more stringent test for utility, requiring a specific application for the gene sequence beyond mere use as a research tool. By

[82] Looney, above n 59, 269.

focusing on the function and application of a genetic sequence, as well as limiting broad patent grants, the patent system will encourage investment, but not hinder research.

Part B: Ownership of Genetic Material and Human Tissue

10. Introduction

Tissue is routinely stored in hospitals or laboratories after surgery or pathology tests have been completed. Tissue may also be taken from participants in experimental trials in hospitals, universities, academic institutions and pharmaceutical companies. Who owns this tissue? Can it be used in research or in different research projects than those for which it was first collected? Can it be bought and sold; or stolen? Who can get access to it? Whose consent is required? Who should share in the proceeds if a profitable discovery is made from research on the tissue? Do the same rules apply to tissue collected for genetic registers to assist families to establish their genetic pedigree and assess risks for genetic conditions? These questions raise complex issues of property in genetic material and human tissue. Many are discussed below.[83]

This part of the paper commences with an outline of the Australian law, then describes the law in the United States and Europe. It sets out and evaluates the arguments for and against recognising a property interest in tissue and information derived from it. It explains some recent recommendations of professional bodies concerning the procedures to be followed in genetic testing (they require information and consent but stop short of recognising a property interest). Finally, the paper describes some recent Australian proposals to regulate genetic testing (especially the Genetic Privacy and Non Discrimination Bill 1998 (Cth)); and lists some legal options for regulation.

10.1 An example - *Moore v Regents of the University of California*[84]

In 1976, John Moore was suffering from hairy cell leukemia. His physician, Dr David Golde, recommended that Moore's enlarged spleen should be removed to slow down the disease. Without telling Mr Moore, Dr Golde retained parts of the spleen for research purposes and developed from them a valuable cell line that was subsequently patented. The cell line contained Moore's DNA. Did he own it? Did he have other property rights in it? Is he entitled to share in the proceeds of its distribution and use?

11. Law in Australia

11.1 Legislation

There is no Australian legislation specifically on ownership of biological material and tissue samples but all jurisdictions have human tissue legislation that is indirectly relevant.[85] This legislation deals with the donation of tissue for specified purposes,

[83] Issues of ownership arise in many other areas, such as forensic DNA banks, and IVF technology. These are not considered in this paper.

[84] *Moore v Regents of the University of California* 793 P 2d 479 Cal (1990).

[85] *Human Tissue Act 1982* (Vic), *Human Tissue Act 1983* (NSW), *Transplantation and Anatomy Act 1979* (Qld), *Human Tissue Act 1985* (Tas), *Human Tissue and Transplant Act 1982* (WA), *Transplantation and Anatomy Act 1983* (SA), *Transplantation and Anatomy Act 1978* (ACT), and the *Human Tissue Transplant Act 1979* (NT).

including medical and scientific purposes. It does not state that donated tissue is property but it recognises the value of tissue and facilitates an arrangement where tissue can be the subject of a gift or bailment.[86] The Acts provide for consent to donations and they prohibit people from buying and selling tissue, including blood.[87] The ban on sale protects tissue supplies from contamination by samples from impoverished or unhealthy donors and reduces risk to recipients.[88]

11.2 Common Law

The common law has come to recognise that body parts may constitute property but there is no case law directly on the ownership of body parts. Initially, a long line of English cases[89] concerning the legal status of human corpses established that there was no property in a dead body. That rule prevented the recognition of proprietary rights in body parts, as parts removed from a body are similar to a corpse. However, in 1906 the High Court of Australia accepted in principle that a human body could be the subject of property (*Doodeward v Spence* (Griffith CJ)); [90] and that approach gained momentum in later cases. In *R v Rothery,*[91] a defendant who removed a blood sample after a blood alcohol test was found guilty of theft. In *PQ v Australian Red Cross Society*[92] the Supreme Court of Victoria accepted that blood products were goods under the *Trade Practices Act* 1974. But the question of ownership remains untested.

In the situation illustrated by *Moore's* case above, where a doctor removes tissue without telling a patient and later develops a profitable product from it, it is conceivable that a court might acknowledge the patient's interest on the principle that the doctor breached a fiduciary obligation to the patient. Although the High Court of Australia said in *Breen v Williams*[93] that the doctor-patient relationship is not a fiduciary one, the court recognised that a doctor owes a patient certain fiduciary obligations. One such obligation is that the doctor should not gain a financial benefit from the relationship with the patient without telling the patient first. That principle might lead to a similar outcome to that in *Moore* (see below), if such a case were litigated in Australia.

11.3 Guidelines

11.3.1 The *National Statement on Ethical Conduct in Research Involving Humans* (1999) published by the National Health and Medical and Research Council (NHMRC) requires that genetic information or material must not be used without the consent of the person concerned, after full information about what is proposed has been

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[86] R Magnusson, 'Proprietary Rights in Human Tissue' in NE Palmer and E McKendrick (eds), *Interests in Goods* (2nd ed, 1998) 43.

[87] *Human Tissue Act 1982* (Vic) s38, *Human Tissue Act 1983* (NSW) s 32, *Transplantation and Anatomy Act 1979* (Qld) s 40-44, *Human Tissue Act 1985* (Tas) s 27, *Human Tissue and Transplant Act 1982* (WA) s29, *Transplantation and Anatomy Act 1983* (SA) s35, *Transplantation and Anatomy Act 1978* (ACT) s44, and the *Human Tissue Transplant Act 1979* (NT) s24.

[88] Magnusson, above n 86, 67.

[89] Originating from *Hayne's case* (1614) 12 Cp. Rep 113; 77 E.R 1389.

[90] (1908) 6 CLR 406.

[91] [1976] Crim L. R 691.

[92] [1992] 1 VR 19.

[93] (1996) 186 CLR 71.

given.[94] However, there are provisions for some research to be undertaken without consent if a Human Research Ethics Committee approves the project and the data is de-identified. It is significant that the NHMRC guidelines do not address the issue of ownership, but nonetheless recognise the interest that an individual has in his/her genetic sample and the importance of privacy and confidentiality.

11.3.2 The NHMRC's *Guidelines for the Use of Genetic Registers in Medical Research* (1991)[95] take a similar approach in requiring prior information and consent before tissue or data are used. The guidelines recommend procedures for collecting data, use of data and release of data. There is no direct reference to the ownership of biological samples stored in genetic registers. Researchers may use stored tissue in certain circumstances with the approval of the keeper of the register and consent from the person concerned. They must ensure security and confidentiality of the information.[96] The guidelines do not explicitly discuss ownership but acknowledge that there is a unique position of trust between the subjects and the keeper of the register, and that special care must be taken to ensure that research does not endanger or exploit that special relationship. In addition, the guidelines set out a number of considerations which should be considered in determining whether consent should be waived.[97]

11.3.3 Anti-Cancer Council of Victoria Guidelines - *Lovell Report*.[98] A different approach was taken by the Cancer Genetics Ethics Committee of the Anti-Cancer Council of Victoria in its report, *Ethics and Familial Cancers*, 1996. It sees tissue as adjunct to the patient's medical records[99] (which are the property of the person who prepared them, not the patient); and tissue specimens, which also, like other laboratory materials, belong to the body holding the material, and not the person concerned. Thus in state public hospital laboratories, property in the tissue would vest in the government of the state or territory. In private laboratories, it would vest in the body under whose auspice the laboratory functions.[100] The guidelines thus state that "inquirers should understand that records, including tissue specimens sent for DNA testing, are the property of the bodies that make the records or hold the tissues".[101]

11.3.4 Contractual arrangements: Human Genetics Society of Australia. Whatever the general law concerning ownership of genetic material, that can presumably be clarified or altered by contract between the parties. The Human Genetics Society of Australia has a generic consent form for a presymptomatic genetic test in its *Guidelines for DNA Predictive Testing*. The consent form includes a statement that the

[94] Chapter 15. These Guidelines are available on the NHMRC web site <http://www.health.gov.au/nhmrc>

[95] These guidelines are currently being updated. The 1991 version and the new draft are on the NHMRC's web site.

[96] NHMRC, *Guidelines for the Use of Genetic Registers in Medical Research* (1991), 5.

[97] Ibid paragraph 15.8.

[98] Anti-Cancer Council of Victoria - Cancer Genetics Ethics Committee, *Ethics and Familial Cancers* (1996), later referred to as the Lovell report. The underlying philosophy of the report is described by L Skene 'Patients' rights or family responsibilities? Two Approaches to Genetic Testing' (1998) 6(1) *Medical Law Review* 1-41.

[99] Lovell report, above n 98, para 7.28.

[100] Ibid para 7.23.

[101] Ibid 59.

blood or tissue tested has been voluntarily given to the testing laboratory and that DNA remaining after the test is done will be the property of the testing laboratory and will be stored in good faith. In addition, the guidelines provide that the testing laboratory will not use DNA samples for purposes other than those agreed in the consent form. The contractual transfer of rights in relation to the tissue avoids the issue of whether it is property and all the legal difficulties that arise from so characterising it.[102]

12. Law in other countries

12.1 United States

In the United States, the notion of property rights in cells removed from the body has been rejected at common law, but several states have legislated to provide for property interests in tissue.

12.1.1 Common law. The facts of the principal case, *Moore v Regents of the University of California*[103] have been mentioned above. Moore's claim was rejected on a preliminary motion at trial but, on appeal, the California Court of Appeal found that he had retained a proprietary interest in his cells, and so was entitled to compensation for conversion. On further appeal, the Supreme Court of California overturned the decision of the Court of Appeal, ruling that Moore had no proprietary interest in his removed cells and thus could not sustain his action for conversion.[104] The court held that the removal of a person's cells and bodily tissues extinguishes a patient's property interest in his cells and genetic material.[105] The court, in justifying its decision, argued that to hold otherwise would restrict access to the raw materials that are needed for research, both legally and as a practical matter, having a detrimental effect on the emerging biotechnology industry.[106] The majority in this case drew on the patent grant stating that the fact that a patent had been issued showed that the tissue in question could not possibly belong to Moore.[107] The majority found that patients' rights are best protected by imposing fiduciary obligations on surgeons towards patients, the result being, in American law, that removed tissues cannot be used without the patient's consent.[108] In acknowledging the complexity of the issue, the California Supreme Court left the final disposition of such complex policy matters to the legislature.[109]

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[102] L Skene 'Patients' rights or family responsibilities? Two approaches to genetic testing' (1998) 6(1) *Medical Law Review* 1,40.

[103] *Moore*, above n 84.

[104] Moore's claim against Dr Golde and the University of California had 13 causes of action, including conversion of bodily property, lack of informed consent, breach of fiduciary duty, fraud, unjust enrichment, and negligent misrepresentation.

[105] *Moore*, above n 84, 488-89.

[106] M Lin, 'Conferring a Federal Property Right in Genetic Material: Stepping into the Future with the Genetic Privacy' 1996(2) *American Journal of Law and Medicine* 109, 118.

[107] *Moore*, above n 84, 492-93. Note that there is an inherent problem in the court's argument as the patent granted was for the process or procedure for creating some new, useful invention, not the cells themselves.

[108] S Huynen, 'Biotechnology - A Challenge for Hippocrates' 1991(6) *Auckland University Law Review* 534, 535.

[109] *Moore*, above n 84, 496. See also Lin, above n 106, 109.

12.1.2 Legislation. Some states have legislated to regulate the accessibility and use of genetic information and genetic discrimination.[110] The legislation is in the form of model Genetic Privacy and Non-Discrimination Bills developed at a federal level.[111] However there is no legislation that specifically addresses the issue of property rights in biological material.

12.1.3 Practice in DNA Banking. The number of DNA samples banked in the United States is rapidly increasing;[112] but the banks often have no written agreement concerning rights over the tissue.[113] Where such agreements exist, they do not state that individuals retain ownership interests in the samples or provide for monetary compensation in the event that research results in the development of commercially valuable products.[114]

12.1.4 Recent federal proposals for legislation. There have been a number of proposals for legislation in the United States in addition to the model Bill mentioned above. These have emanated from concerns about the privacy of genetic information and the potential misuse of that information. Some contain provisions about ownership.

The *Genetic Privacy Bill* 1995 (US), for example, has been presented to the United States Congress but not passed. It not only prohibits the collection of an individually identifiable DNA sample without the written authorisation of the sample source,[115] but it also states that an individually identifiable DNA sample is the *property* of the sample source.[116] This is a major reason why the bill has not been passed.

The *Genetic Confidentiality and Nondiscrimination Bill* 1997 (US) has also been presented to the United States Congress but not passed. It does not confer a proprietary right to genetic material, but still legislates extensively to protect an individual's interest in his/her genetic material. For example, a tissue sample may not be collected unless, prior to collection, the donor is given a written notice of rights and assurances which states, amongst other things that:

- the DNA sample will be used only as authorised in the written authorisation
- the individual has the right to order the destruction of an identifiable DNA sample at any time

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[110] Lin, above n 106, 130.

[111] The underlying philosophy of these Bills is described by L Skene, above n 102.

[112] A study as early as 1994 revealed that 90% of the 148 DNA diagnostic labs surveyed had begun to bank DNA. Over half of these had already accumulated 500 samples or more: J McEwan and P Reilly, 'A Survey of DNA Diagnostic Laboratories Regarding DNA Banking' (1995) 57 *American Journal of Human Genetics* 1477.

[113] The study above (note 112) found that 35% of the laboratories holding tissue had no written internal policies regarding any aspects of DNA storage, and more than half were without any type of written depositor's agreement.

[114] Ibid.

[115] *Genetic Privacy Bill* 1995 (US) s101(a). This is similar to other regulatory instruments and guidelines. It also states that the written authorisation must satisfy specific requirements to remain valid, such as identifying the collector, containing instructions for the sample after analysis, and stating the authorised uses for the sample: s 103.

[116] Ibid, s 104(a).

- the DNA sample will be destroyed upon the completion of the genetic analysis or the genetic test, unless the individual has consent in writing to further use of the sample
- researchers may be granted access to a DNA sample only as specified in the written authorisation
- the collection, storage, and analysis of the DNA sample and the genetic information characterised from the sample are protected by the Act
- an individual whose rights under the Act are violated may seek civil remedies.[117]

12.2 Europe

Most countries in Europe have legislation on organ transplantation[118] but very few have legislated with respect to human tissue.[119] Those that have legislated on human tissue include Belgium, France, Spain, Macedonia and Austria. Most countries prohibit tissue collection for commercial purposes. A report funded by the European Commission in 1992 found that in no European country was a citizen granted full ownership of his/her genetic material.[120] This report further noted that the concept of ownership is not often used in Europe with regard to body material. Nonetheless there is support for varying degrees of control by the individual over the body and bodily parts.[121] This is illustrated by the Council of Europe's Committee of Ministers Statement on Genetic Testing and for Health Care. Principle 13 states that:

"Samples collected for a specific medical or scientific purpose may not, without permission of the persons concerned or the persons legally entitled to give permission on their behalf, be used in ways which could be harmful to the persons concerned."

Furthermore Principle 8 provides that:

"The collection and storage of substances and samples ... must be in conformity with the Council of Europe's basic principles on data protection laid down in the Convention for the Protection of Individuals with regard to Automatic Processing of Personal Data."

In general, it can be observed that European countries have avoided recognising proprietary rights in genetic material. Nonetheless, it is clear that the Council of Europe has considered it important that individuals should retain limited control over their samples, and that the collection and storage of samples be regulated.

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[117] *Genetic Privacy and Nondiscrimination Bill 1997(US)*, sec 101.
[118] With the notable exceptions of Germany, Holland, and Switzerland.
[119] O Quintanta, 'Human Tissue Banks in Europe' in B Knoppers (ed) *Human DNA: Law and Policy* (1997) 423.
[120] J de Witte, *Human Genome, Body, Identity and Property: Philosophical Issues* (EC Project PL 9101027, 1992).
[121] R Chadwick, 'The Status of Human Genetic Material - European Approaches' in B Knoppers (ed) *Human DNA: Law and Policy* (1997) 55, 57.

13. Arguments in favour of a proprietary right in human tissue

Sections 2, 3 and 4 below set out the arguments for and against the acknowledgement of a proprietary right in human tissue and then evaluate those arguments.

13.1 Owning one's body is a basic human right and this extends to removed tissue

It is self-evident that people own their own bodies in the sense that no one can lawfully remove anything from a person's body without consent or some other lawful justification. There is no logical reason why the ownership of the body should not extend to tissue samples taken from the body. The recognition of a property right in human tissue is essential if individuals are to maintain sufficient control over their bodies, and be accorded human dignity (see *Moore*[122]).

13.2 Proprietary rights protect autonomy

The ethical principle of autonomy is paramount in medical ethics and law today. This has been acknowledged in many judgments in Australia and other common law countries. It is the basis of legislation such as the Medical Treatment Act 1988 (Vic). People are entitled to make their own decisions about medical procedures and to be provided with information to enable them to make an informed choice. This right to control and decide about their bodies extends to deciding what may be done with their tissue. Genetic testing allows access to private medical information about an individual. People are concerned about this information being used by insurers and employers to discriminate against individuals. Recognising a proprietary right in human tissue is the best way to protect people's autonomy, privacy and confidentiality.

13.3 Human biological material is already property

Stating categorically that human tissue cannot be subject to proprietary rights suggests that it could not be gifted, bought, sold, stolen, converted, bailed or patented, in the absence of specific empowering legislation.[123] That is contrary to current practice. Physicians, researchers, and pharmaceutical companies already exchange such material, increasingly for a fee, and apply for, and receive patents for such material.[124] There are therefore ample grounds for concluding that human tissue, like other commercial goods, can be the subject of proprietary rights.

13.4 Proprietary rights will encourage scientific research

Acknowledging property rights in biological material will advance, not hinder, the biotechnology industry. It will promote future investment and scientific research. The reason is that proprietary rights provide an incentive for people to supply biological

[122] This argument was advanced by Justice Mosk in his dissent in *Moore*, above n 84.
[123] Magnusson, above n 86, 25.
[124] Moore, above n 84, 160.

material. Without the inducement of a property right, they may be reluctant to allow their tissue (or themselves) to be used for laboratory or clinical research purposes. Having more samples increases a researcher's chance of success because the best samples can be selected.

14. Arguments against proprietary rights in human tissue

14.1 Proprietary rights will restrict research

Recognising proprietary rights in human tissue will impede scientific research and development.[125] Every researcher who uses tissue samples in research could be held liable in conversion unless the donor previously agreed to that use. Although donors can be "revisited" for their specific consent, that can be difficult in practice.[126] Researchers will naturally be reluctant to use tissue if there is a risk of liability. This will deter investment and the development of new pharmaceutical products.

14.2 Proprietary rights will prejudice health care

If genetic registers and the tissue associated with them are not freely available to all blood relatives, some may be deprived of information they need for their health care. If people have a property right in stored tissue, their consent will be required before access to tissue or information can be granted. Providing adequate information and obtaining consent in every case will be cumbersome and expensive.[127] Also people could veto access. For this reason, one major policy committee recommended that a person whose tissue is taken and tested for familial cancer should not be entitled to prevent access when that is necessary for the health of another relative.[128]

14.3 Proprietary rights will encourage trade in tissue

Recognising property rights in human tissue will make tissue nothing more than a tradeable commodity. Trading in human flesh takes us back to the days of slavery. The poor and disadvantaged will be further victimised by being forced to sell their organs.[129] Tissue supplies will then be contaminated by diseased and unhealthy samples. Also, selling body parts to the highest bidder is unjust. All people have an equal right to treatment, irrespective of their wealth.[130]

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[125] R Gold, *Body Parts Property Rights and Ownership of Human Biological Materials* (1996) 26. Citing the majorities reasoning in *Moore*.
[126] L Skene, above n 102, 33.
[127] Ibid 26.
[128] Ibid 27.
[129] S Mortinger, 'Spleen for Sale: *Moore v Regents of the University of California* and the Right to Sell Parts of Your Body' (1990) 51 *Ohio State Law Journal* 499, 508-509.
[130] Huynen, above n 108, 541.

15. Evaluation of arguments concerning ownership of tissue samples

Most policy committees have stopped short of recommending, as a general proposition, that a property interest should be recognised in human tissue. There is good sense in this. Imagine the complex issues that may arise if tissue is legally regarded as always being owned by the person from whom it was taken. If the person dies and the tissue is still stored in the hospital laboratory, will it pass to the person's heir under a will or on intestacy? And under what legal principle does the hospital acquire the tissue in the first place? Is it a bailment? Can the person demand that the tissue be returned after "use"? Can it be sold? If it is stolen or destroyed in a laboratory fire, can the person claim compensation on the hospital's insurance policy? What financial value could be placed on tissue (say a test tube filled with oesophageal tumour cells) in such circumstances? These are lawyers' questions arising from the basic principles of property law but the mere statement of them indicates the oddity of a general rule that tissue is the property of the donor.

Also, such a principle seems undesirable from a policy perspective, at least in relation to tissue held in hospitals after diagnostic tests. The intention of the parties in this case is surely that the tissue should be used for the patient's diagnosis and treatment. This obviously covers its use in the initial diagnostic test and perhaps for repeat testing soon afterwards. It may even be argued to extend to later tests by the hospital; for example, quality assurance measures to check the accuracy of testing procedures, since that testing may also be for the patient's benefit, albeit longer term. (If the test is shown to be faulty, the patient can be contacted and re-tested). However, use of the tissue in research is more difficult to justify on the basis of the original intention or an implied consent, since the benefit to the patient is less evident and immediate. But, even if the person obtains no benefit from the research, what harm is there if the tissue is used in a codified or anonymised form? Could one not apply a utilitarian approach and say that on a risk-benefit analysis, the limited invasion of the donor's privacy right is outweighed by the potential benefit of the research?

Civil libertarians certainly place a high value on the mere use of tissue without specific consent, even in the absence of any demonstrable harm to the person concerned. Does the public at large take the same view? Could one not take a communitarian perspective and argue that, as members of a community, we have an obligation to contribute to the general good where that involves no harm to us personally?

The effect on research if property rights are - or are not - recognised in tissue seems moot. On the one hand, it may encourage donors to come forward, or to consent to the use of stored samples. On the other, it imposes additional costs in gaining approval from ethics committees, informing donors, obtaining and documenting consent, reporting back to institutional and central ethics committees and the like. When the impact of the latter requirements is considered in more detail (the various steps, the number of people involved, the bureaucracy), it seems that research would be better encouraged by non-recognition of a property right in the tissue.

Even if a general property right is not acknowledged, there remains the issue of tissue (like blood products) that are already bought and sold, for example by the Australian Red Cross. There are good therapeutic and humanitarian reasons for allowing this type of sale. How is this different from a general principle that there can be no property in tissue? Could one argue simply that this is an exceptional case? Or that property rights can be acquired when tissue is "processed" in some way? Does it make a difference that the donor has consented to the use – or that the use is directly therapeutic?

Throughout any policy analysis, one should remember the concerns that people have about the use of tissue without consent. They are worried about being exploited – or about possible repercussions for them if personal information is wrongly used or revealed in the public domain. There are other responses to these concerns. First, doctors and researchers have common law duties in trespass and negligence to obtain consent for medical procedures and to provide information about what is proposed before the patient agrees. Secondly, the High Court of Australia has recognised the existence of fiduciary obligations on the part of doctors which prevent them obtaining a financial reward for themselves without informing the patient (*Breen v Williams, supra* although there is little Australian law to date on that aspect). Thirdly, ethical guidelines of bodies like the National Health and Medical Research Council recommend that tissue should not be used without consent unless that is coded or anonymised; and the research is approved and overseen by Human Research Ethics Committees. If necessary, other methods could be developed to protect patients' interests and assuage doubts about doctors or researchers gaining an unfair advantage from using patients' tissue without consent. (These might include fuller information requirements; or an "opting out" facility.)

Finally, one should distinguish between the use of tissue for therapeutic and research purposes. The former includes procedures such as establishing an index case for genetic diagnosis; conducting genetic linkage within a family; preparing a family pedigree; and running a genetic register. In all of these circumstances, there is a stronger argument for denying a right of veto over the use of tissue where that can directly benefit other blood relatives. The reason is that one has greater obligations to one's family than to the world at large; and the benefit of knowing about the genetic risk is more immediate and direct than the potential benefits of research.

For reasons such as these, commentators have generally focussed on the right of donors to autonomy – not to have things done to them without being properly informed and without their consent. This right to autonomy has been emphasised, rather than a right to privacy (not to have their tissue secretly used); or a right to property in the tissue (a right to control its use; or to buy and sell it). The right to autonomy could be supported by fuller disclosure requirements before the tissue is taken, perhaps with a general statement that stored tissue may be used in research without further reference to the donor on an anonymised basis and subject to the supervision of a Human Research Ethics Committee. Although it is conceivable that living DNA might be preserved and reproduced indefinitely in a therapeutic form such as a cell line that encodes personal details of the particular donor, it would be of little significance since that person could not be identified.

16. Recommendations by Professional Bodies

Many professional bodies have published guidelines recommending procedures to be followed in taking tissue for genetic testing and for the storage of tissue and genetic information. These guidelines focus on the need to provide information to the person concerned and to obtain consent to the taking, storage and use of tissue and information. Although some approve the use without consent for research in limited circumstances, that can only be done if the information is de-identified (ie coded but the donor can be traced if necessary); or anonymous (all identification severed). The guidelines that are specifically directed to research are more stringent in restricting access than those dealing with genetic registers, which are more concerned with sharing information among family members for health reasons. The guidelines include the following.

16.1 The American College of Medical Genetics, *Statement on the Storage of Genetics Materials* (1995)[131] does not refer to the ownership of genetic material. It recommends that certain matters should be clarified when samples are obtained for clinical tests. These include:

- the anticipated use of samples
- the scope of permission to use samples or results in counselling and testing relatives and if so, which relatives
- the permission to use samples in research if identifiers have been removed including the type of research
- the duration of storage of genetic materials.

16.2 The American Society of Human Genetics, *DNA Banking and DNA Analysis: Points to Consider* (1996)[132] states that:

- banked DNA is the property of the depositor unless otherwise stipulated
- deposited DNA may be used for purposes unrelated to the original request of the depositor only with his/her express consent
- DNA banks should only disclose the result of a DNA test to a third party with the express consent of the individual.

16.3 The Human Genome Organisation (HUGO) Ethics Committee, *Statement on DNA Sampling: Control and Access*[133] did not acknowledge an express right of ownership. It said that:

- tissue taken and stored for medical care may be used for research if there is general notification of such a policy, the patient has not objected, and the sample has been coded or anonymised
- tissue taken before notification of the policy may be used for research if the sample is anonymised

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[131] American College of Medical Genetics, 'Statement on Storage and Use of Genetic Materials' (1995) 57, *American Journal of Human Genetics* 1499-1500.

[132] American Society of Human Genetics, 'Statement on Informed Consent for Genetic Research' (1996) 59 *American Journal of Human Genetics* 471-474.

[133] Human Genome Organisation Ethics Committee, *Statement on DNA Sampling Control and Access* (Feb 1998). Available on the web at <http://www.gene.ucl.ac.uk/hug/sampling.html>

- tissue taken for research (and its information) can be used if people consent, either to identified use, de-identified use or anonymous use
- research samples obtained with consent and stored may be used for other research if there is general notification of such a policy, the participant has not yet objected, and the sample is coded or anonymised.

16.4 The World Health Organisation, *Proposed International Guidelines on Ethical Issues in Medical Genetics and Genetic Services* (Dec 1997)[134] state that the most efficient approach to consent for genetic registers is a blanket informed consent that allows the use of samples in future projects. The guidelines say that:

- control of DNA may be familial, not only individual
- blood relatives should have access to stored DNA to learn their genetic status, but not to learn the donor's genetic status
- DNA should be stored as long as it can be of benefit to living or future relatives or foetuses
- no one should have access without the donor's consent, except for forensic purposes or where the information is directly relevant to public safety
- insurance companies, employers, schools, government agencies and other institutional third parties (who may be able to coerce consent) should not be allowed access, even with the individual's consent.

16.5 The Australian National Health and Medical Research Council (NHMRC), *Draft Guidelines for Genetic Registers and Associated Genetic Material* (1999) comprehensively cover the operation of genetic registers in Australia. They replace earlier guidelines that were amended following criticism by the Privacy Commissioner in his report entitled *The Privacy Implications of Genetic Testing* (1991).[135] The guidelines cover the establishment of registers, recruitment of registrants, consent and confidentiality, security of registers, and amalgamation and winding up of registers. There is no express right of ownership but the following information must be given before consent to the taking and storage of tissue, or the inclusion of the person on the register:

- what information and genetic material is collected and stored[136]
- the intended duration of storage (consent should include consent to dispose of the material at the end of that time;[137] and register staff should check to see if the registrant still agrees before disposing of the material)[138]
- what should be done with identified information and stored genetic material after death[139]
- the register's guidelines for ensuring confidentiality of information and protection of registrants' privacy[140]

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[134] Available on the internet at <http://www.who.int/ncd/hgn/hgnethic.htm>

[135] Privacy Commissioner, *The Privacy Implications of Genetic Testing: Information Paper number Five* (1996).

[136] NHMRC, *Draft Guidelines for Genetic Registers and Associated Genetic Material* (1999), 12.

[137] Ibid 5.2.1.(b)

[138] Ibid 5.2.1 (b)

[139] Ibid 5.2.1 (c)

[140] Ibid 5.1 (viii).

- who is denied access to identified information and genetic material eg. insurers, employers, family members who do not have the registrant's permission for access.

17. Recent Australian developments

17.1 Genetic Privacy and Non Discrimination Bill 1998 (Cth)

Senator Stott-Despoja (Dem) introduced this Bill into the Senate in 1998. As she said in the Second Reading speech, "The provisions are a balance between the interests of complete ownership and promoting the opportunity of researchers to derive a commercial benefit from their endeavours". The Bill is similar to the US model *Genetic Confidentiality and Nondiscrimination Bill* 1997 (and also to the recommendations of the professional bodies described above) in requiring information and consent before tissue is collected, stored or used.[141] But it goes further by envisaging that people may be entitled to share in the proceeds if their tissue or information is used to develop a commercial product. This is not exactly a property interest but it does have financial value. Yet the Bill also provides for research on tissue without consent in certain circumstances (see below), if the use is anonymous. That would not be possible if the donor owned it.

The Bill requires that tissue must not be taken, tested or stored without prior written authorisation from the donor[142] and that the donor must also be given a notice of rights and assurances. There are specific requirements for each of these.

The *written authorisation* must state:
- all authorised uses of the DNA sample[143]
- whether it may be used in research
- whether it may be used commercially, with a waiver of, or provision for, economic benefit to the individual[144]
- the option of supplying the sample in a de-identified format.[145]

The *notice of rights and assurances* must state:
- the DNA sample will be used only as authorised[146]
- the donor may order the sample to be destroyed[147]
- the sample will be destroyed after the test unless the donor gives written consent for further research[148]
- the donor may appoint someone else to decide about disposing of the sample[149]
- the donor has the right to examine records[150]

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[141] *Genetic Privacy and Non-discrimination Bill* 1998, Part 3, clause 12.
[142] Ibid clause 16(1)(a)
[143] Ibid clause 16(1)(d)
[144] Ibid clause 16(1)(f)
[145] Ibid clause 16(1)(f)(iii)
[146] Ibid clause 14(a)
[147] Ibid clause 14(b)
[148] Ibid clause 14(c)
[149] Ibid clause 14(d)
[150] Ibid clause 14(e)

- researchers may get access only as permitted by the written authorisation[151]
- storage and analysis of the DNA sample and the genetic information characterised from the sample are protected
- an individual whose rights are violated may seek redress.[152]

DNA samples may be used in research without consent in limited circumstances; ie if:
- the sample is essential to the project
- the potential benefit of the research to society outweighs the potential risk to research subjects[153]
- the research protocol provides adequate safeguards to protect privacy;[154] at a minimum this means satisfying any guidelines issued by the NHMRC, and approved by the Privacy Commissioner[155]
- it ensures that research subjects are not identifiable in any report or publication[156]
- it has procedures to remove or destroy any individual identifiers at the earliest opportunity.[157]

17.2 Senate Report on the Genetic Privacy and Non Discrimination Bill 1998 (1999)

The Genetic Privacy and Non Discrimination Bill 1998 was referred to the Senate Legal and Constitutional Legislation Committee, which reported in March 1999. This Committee said that the Bill dealt with the relevant issues but some required further consideration and consultation, particularly ownership of genetic material; and ownership of information derived from such material.[158]

The Committee said that there are legitimate interests on all sides in medical research – researchers, pharmaceutical companies, indigenous groups and individuals. Regulation is needed to clearly enunciate the policy position that is to be adopted and to ensure that justice is done to individuals and groups of people who may otherwise be commercially exploited. Also, from the perspective of public policy, it is desirable that a lack of regulation does not prompt people and groups of persons to refuse to participate in research because their interests are not recognised by the law.[159]

In general, the Committee said, medical research in Australia is well regulated. There are adequate safeguards to ensure that research is conducted appropriately. However, there is some doubt about whether research funded in the private sector is covered by the NHMRC guidelines.[160]

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[151] Ibid clause 14(f)
[152] Ibid clause 14(g)
[153] Ibid clause 20(1)(a) and (b).
[154] Ibid clause 20(c)(i).
[155] Ibid clause 20(2)(a)
[156] Ibid clause 20(2)(b)
[157] Ibid clause 20(2)(c)
[158] Senate Legal and Constitutional Legislation Committee, *Report on the Genetic Privacy and Non Discrimination Bill 1998* (1999), para 4.41
[159] Ibid para 4.39
[160] Ibid para 4.40

18. Policy Options

18.1 Legislate to recognise a proprietary right in human tissue

If it is decided that a proprietary right should be recognised in human tissue, one could legislate to establish such a right with provisions similar to the Genetic Privacy Bill in the United States (para 3.1.4 above). People would then be able to capitalise on commercial enterprises resulting from scientific research on cells they provide. Also, it would provide additional protection from genetic discrimination resulting from unauthorised use of their samples.

This would need to be balanced against added costs and practical difficulties for scientists undertaking research and the impact for the community as a whole. The issues raised above concerning the legal implications of recognising a property interest (para 15) must also be considered. Also, are property interests appropriate when tissue is collected for therapeutic purposes, such as genetic registers, rather than for research from which the donor – or the donor's family - will obtain no special benefit?

18.2 Legislate to regulate the area, but do not recognise a proprietary right in tissue

A second option to protect the interests of tissue donors is to legislate to regulate the use of genetic samples, without expressly recognising a proprietary right in human tissue. This is similar to the recommendations of the various professional bodies concerning tissue used in research (paras 7.1-7.3 above), focussing on the need for full information and consent. It could be achieved by enacting legislation like the Genetic Privacy and Non-Discrimination Bill 1998 (Cth) (para 8.1 above), excluding the provision for sharing in profits of use of tissue.

This option has the advantage of not commercialising organ or tissue donation, while at the same time protecting people from potential exploitation. Laws restricting disclosure of information and access to samples will protect an individual's privacy and confidentiality. Legislation, of course, has the advantage of direct enforceability. It can establish regulatory bodies to oversee compliance and impose penalties. This would meet the concern that the NHMRC guidelines may not apply to private agencies.

But is legislation really necessary when the present system of guidelines administered by the NHMRC seems to be working well? And, if legislation is desirable, would it not be better restricted to anti-discrimination or privacy legislation directed to the wrongful *use* of the information, rather than legislation that imposes burdensome bureaucratic requirements every time tissue is taken for health purposes?

18.3 The status quo: regulation by guidelines of NHMRC and professional bodies

Currently most hospitals and academic institutions which bank human tissue samples are regulated by Human Research Ethics Committees (HRECs), which are in turn bound

by NHMRC guidelines. The Australian Health Ethics Committee (AHEC), one of the principal committees of the NHMRC, oversees the guidelines and the activities of HRECs. AHEC is a diverse body with representatives from all sectors of the community. HRECs are also widely based, with representatives from outside the institution. In addition, there are professional guidelines that recommend procedures for genetic testing and there are similar indirect legal inducements to comply with them.

Although these guidelines do not have legislative backing, they are likely to be observed. Compliance is a condition of funding in NHMRC funded projects. The guidelines are an indication of accepted practice in proceedings for negligence or breach of contract. Breach might be unprofessional conduct in disciplinary proceedings. Even if the guidelines are not directly incorporated in a contract of employment, it is expected that they will be observed and a breach might impede career advancement or publication prospects. In short, non-statutory guidelines do have teeth! This applies even if the research is not funded by the NHMRC so that it is not covered by the guidelines. The guidelines are still an indication of accepted practice and could be taken into account in litigation or disciplinary proceedings. Guidelines also have the advantage of flexibility. Given the accelerating pace of biotechnological innovation this is a substantial advantage.

On the other hand, guidelines cannot compensate someone whose tissue is used in a profitable enterprise without the person's consent. A further concern is the possibility of future litigation based on alleged property rights. The legal uncertainty may deter investors from investing in scientific research. However, if anonymity is preserved in using tissue commercially, there seems little scope for this.

18.4 Establishment of a Royalty-Based Clearinghouse system

A proposal that has arisen in the United States is a royalty based system similar to that of the Performers Rights Association, which privately calculates and distributes royalties to the music industry. With respect to biological raw materials, a similar system could be set up wherein patient-donors sign up with a "clearinghouse" that would distribute the cells, tissues, and other biological materials. The clearinghouse could then charge the industry for access to these raw materials. It has been argued that such a system would be a feasible alternative to the legislative or judicial recognition of proprietary rights in genetic material.[161] An advantage of this system is that it would provide a central point for sample collection, and would also compensate individuals for commercial exploitation of their genetic material. However, it would not cover the whole field of stored tissue, including genetic registers.

18.5 Regulation by Contract

It has been proposed that the issue of whether a research institution owns a DNA sample should be regulated by a contract between the donor and the institution. An individual contracting with an institution could, for example, transfer all rights concerning the tissue subject to an undertaking by the storage facility that it will provide information,

[161] Lin, above n 106, 121.

or make samples available for testing by blood relatives. Furthermore a contract could bind an institution to conduct research according to established ethical practices, supervised by an ethics committee.[162] It has been noted that the contractual transfer of rights in relation to the tissue avoids the issue of whether it is property and all the legal difficulties that arise from so characterising it.[163] Critics argue that such a system promotes standardised contracts that do not recognise an individual's rights with respect to a tissue sample.

19. Conclusion

Recognising a general property right in tissue raises difficult legal issues. Some are abstract or technical, such as the legal basis on which a hospital or laboratory acquires tissue for testing; and the donor's subsequent rights in relation to its use and disposition. Others are more significant from a commercial perspective, such as the donor's right to share in the proceeds if a valuable product is developed from the donor's tissue, cells or DNA.

Most government instruments, guidelines, policy recommendations and commentators, both in Australia and other countries, have not recommended recognising a general property right in tissue. Instead, they have focussed on the autonomy rights of the donor, sometimes advocating fuller disclosure of information, or the provision of a statement of rights and responsibilities, before the initial removal of tissue.

If tissue is later used in research without the donor's consent, ethical guidelines in Australia and other countries recommend that information derived from the tissue should be coded or anonymised; and that approval should be sought from institutional ethics committees which must supervise on an ongoing basis. In Australia, these committees are Human Research Ethics Committees under the aegis of the National Health and Medical Research Council (NHMRC). For research funded by the NHMRC, there are direct and indirect inducements to comply with the guidelines. For research funded from other sources, the guidelines provide a guide to accepted practice and might have indirect legal effect. This form of non-statutory regulation is in line with that for other types of medical and scientific research and there is no reason to believe that it is not working well.

It is true that there are anomalies in the current law, such as the judicial recognition that blood and blood products are goods under the Trade Practices Act and may be bought and sold – obviously suggesting a property interest. However, those anomalies would not seem to justify major amendment of the existing law to categorise tissue as property in all circumstances. Concerns about potential misuse of tissue and genetic information derived from it can largely be met by requiring that research undertaken without the donor's consent must be coded or anonmyised; and that it is part of a doctor's fiduciary obligations towards the donor to ensure that that occurs.

[162] Skene, above n 102, 39.
[163] Ibid.

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Part C: Position of the Law Institute of Victoria

Biological patents

Australian law should continue to permit patents of human genetic material and applications of that material provided the basic requirements of utility and novelty are met. If any change is made, it should be limited to a more stringent test for utility, requiring a specific application for the gene sequence beyond mere use as a research tool.

The reasons for this recommendation are as follows:

1. Patents encourage research and the development of new products.
2. Australia has much to gain from the emerging biotechnology industry that is already producing major financial returns in the United States and the United Kingdom. Biological patents are allowed in those countries, as they are in Australia.
3. The Australian Patent Office has a clear policy for granting biological patents. Many have already been granted and there are many more applications awaiting consideration.
4. Australia has international treaty obligations that prevent the refusal of patent protection in Australia.
5. A number of policy committees have considered whether biological patents should be restricted and have recommended that they should be allowed.
6. Patents are not ownership. They apply only for a limited period.
7. A patent holder is not permitted to refuse to allow others to use the patented invention. If that occurs, the Patents Act 1900 (Cth) contains provisions allowing a court application for a compulsory licence to be granted to someone who wants to use the invention.
8. Patents do not encourage secrecy. Patent holders must reveal the details of the invention, together with instructions for reproducing it, before the patent will be granted.
9. Concerns have been expressed about the effect of patenting genetic tools (eg genes and genetic sequences) because paying to use these tools increases research costs for others. However, denying patents for genetic tools reduces the incentive to work on finding new ones. A balance is needed between the interests of researchers working on new genetic tools and researchers wanting to use those tools in their research. This may be achieved by applying a more stringent test for utility, requiring a specific application for the gene sequence beyond mere use as a research tool. By focussing on the function and application of a genetic sequence, as well as limiting broad patent grants, the patent system will encourage investment, but not hinder research.

Use of human tissue for research and patenting

The law should not recognise a general property interest in human tissue (ie that tissue is always being owned by the person from whom it was taken).

If there is legal intervention, it should be similar to the National Health and Medical Research Council's guidelines. That is, tissue taken with consent after full information about the immediate purpose for which it will be used, may be used in research without further reference to the donor on an anonymised basis and subject to the supervision of a Human Research Ethics Committee.

The reasons for these recommendations are as follows:

1. Although the law currently recognises property rights in tissue in limited circumstances, complex legal issues will arise if that is extended to a general right.
2. The current law is adequate to protect people from having their tissue taken, used in research or exploited for commercial purposes:
   - Doctors and researchers have common law duties in trespass and negligence to obtain consent for medical procedures and to provide information about what is proposed before the patient agrees.
   - The High Court of Australia has recognised the existence of fiduciary obligations on the part of doctors which prevent them obtaining a financial reward for themselves without informing the patient (*Breen v Williams*, *supra* - although there is little Australian law to date on that aspect).
3. Ethical guidelines of bodies like the National Health and Medical Research Council also recommend that tissue should not be used without consent unless the research is approved and overseen by Human Research Ethics Committees; and the samples are coded or anonymised. Although these guidelines do not have legislative backing, they are likely to be observed:
   - Compliance is a condition of funding in NHMRC funded projects.
   - The guidelines are an indication of accepted practice in proceedings for negligence or breach of contract.
   - Breach might be unprofessional conduct in disciplinary proceedings.
   - Even if the guidelines are not directly incorporated in a contract of employment, it is expected that they will be observed and a breach might impede career advancement or publication prospects.
   - This applies even if the research is not funded by the NHMRC so that it is not covered by the guidelines. The guidelines are an indication of accepted practice and could be taken into account in litigation or disciplinary proceedings.
4. Guidelines have the advantage of flexibility. Given the accelerating pace of biotechnological innovation this is a substantial advantage.
5. If legal intervention is considered, it should be similar to the guidelines. That is, tissue taken with consent after full information about its immediate use could lawfully be used in research if anonymised and overseen by a Human Research

Ethics Committee. This would provide additional legal protection for researchers. However, litigation is unlikely if tissue is used anonymously.

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SINGAPORE HOSPICE COUNCIL

13 December 2001

Prof. Lim Pin
Chairman
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250 North Bridge Road
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Dear Prof Lim Pin

REQUEST FOR FEEDBACK REGARDING HUMAN STEM CELL RESEARCH IN SINGAPORE

Firstly, please accept my apologies for the delay in replying to the request for feedback.

I had actually given the principal members of the Council time to consider and respond to me individually. To my pleasant surprise we are unanimous in opinion.

The points made are:

1. **Source**

   Concern is expressed over the extraction of stem cells from embryos or feotuses. We would find this most unacceptable. We are pro-life and believe that life begins with fertilization.
   We have less reservation over adult stem cells obtained from tissues such as bone marrow, umbilical cords and brain.

2. **Acceptable uses of stem cells**

   We do not find any ethical issue behind using stem cells as Cells and EG Cells – basically to support life.

3. **Unacceptable uses**

   We are all against the use of stem cells for reproductive cloning of human beings or even therapeutic cloning. We are against cloning or other similar work.

Cont'd /2

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Prof. Lim Pin
Chairman
Bioethics Advisory Committee

13 December 2001

Working on the basic principles above we are concerned over the source for obtaining the stem cells. We would favour existing and new uses of stem cells for supporting life. We are definitely against any form of cloning.

I hope that our response is useful for the deliberations of the Committee.

Thank you.

Yours sincerely,

Gerard Ee
Chairman

GE:sw

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Our Ref: SMA/LCH/cge/BAC/2001

27 November 2001

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Dear Prof Lim

REQUEST FOR FEEDBACK REGARDING HUMAN STEM CELL RESEARCH IN SINGAPORE

Thank you for your letter of 8 November.

The SMA Council is grateful for the opportunity to review the consultation paper prepared by the Human Stem Cell Research Subcommittee.

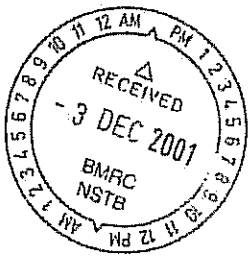
We are pleased to submit our feedback in Appendix 1 from a member.

We appreciate the opportunity to present our feedback.

Yours sincerely

LOW CHENG HOCK
President
Singapore Medical Association

Enc:



SUBMISSION FROM SINGAPORE MEDICAL ASSOCIATION ON THE CONSULTATION PAPER BY THE BIOETHICS ADVISORY COMMITTEE REGARDING HUMAN CELL RESEARCH IN SINGAPORE

Like most cutting edge research, human stem cell research raises a number of difficult and important ethical issues and concerns, requiring the potential benefits to be balanced against the need to protect the rights and welfare of citizens. Based on our limited knowledge and experience, we would like to offer the following comments for the BAC to consider.

1. The view of the Bioethics Advisory Committee (BAC) on embryonic germ (EG) cells echoes those held by in UK and the USA, i.e. that there should be a clear separation between decisions and actions relating to the termination of pregnancy and decisions and actions relating to the use of the foetal material made available. However, it is our humble opinion that explicitly spelt out guidelines, like the Polkinghorne guidelines in UK, should be drawn up to govern the use of foetuses and foetal materials in treatment and research. This should, in particular, include:

    a) the prohibition of directed donation of cadaveric foetal tissue for EG cell derivation. This is necessary to ensure that inappropriate incentives and coercions are not introduced into a woman's decision to have an abortion.
    b) the prohibition of sale of foetal tissue for research purposes. The potential for coercive pressure is greatest when financial incentives are present, and the respect for the moral status of the embryo may be significantly undermined by commercial motive introduced into donation or solicitation of foetal tissue for research purposes.
    c) referral of any research proposal involving the use of foetal materials to a research ethics committee or institutional review board.

2. Much of the debate on the research involving embryonic stem (ES) cells revolves around the moral status of the human embryo, and the level of respect and protection that should be accorded. This is an especially sensitive issue in pluralistic society like Singapore, where different cultural and religious groups may have very contrasting views. The position taken by the BAC parallels the Human Fertilisation and Embryology Act 1990 of UK; the embryo is recognised as a potential rather than a full human being, where the potential benefits of the proposed research can be weighed against the respect due to the embryo. We believe that the key issue here is the public acceptability of such a position, and we are confident that an public policy on stem cell research can be achieved based on widely shared values in our society, carefully weighing the benefits of stem cell research against the need to protect human life. We support therefore the BAC's view that:
    a) the eventual guidelines will need to take into account as wide as possible a spectrum of views and opinion from the community, especially those with medical, religious, scientific, ethical and legal interests.
    b) the need for careful regulation of the proposed research, laying down clearly guiding principles and limits for the research.

3. In our opinion, one contentious issue that the consultation paper did not touch on, as far as the derivation of ES cells is concerned, is the intent involved in producing the embryos. It is the intention to create a child that makes the creation of an embryo a morally justifiable act. Deliberately creating embryos that are disconnected from human relationships takes them out of context and demands for stronger justification than the acquisition of potentially important information. To create embryos solely and with the pre-meditated intention for research seems to cheapen the act of procreation and turn embryos into commodities. Some observers in US have also warned that it can put women at risk as sources for ova for projects that provide them with no benefit. A clear distinction can and should therefore be made between

research using ES cells derived from spare embryos in fertility treatment and research using ES cells created specifically for research. In our opinion, the former is permissible and should be allowed, as long as measures reflecting principles of research ethics are in place, including:

a) clear separation exists between the decision to create embryos for fertility treatment and that to donate the human embryos in excess of clinical need for research purposes
b) physician for fertility treatment should have no financial or professional stake in the proposed ES cell research
c) assurance of voluntariness and absence of inducement, monetary or otherwise
d) informed consent is obtained to the extent permissible
e) individuals undergoing fertility treatment should be approached for consent for donation of human embryos only at the time of deciding the disposition of embryos in excess of the clinical need.
f) directed donation of the embryos must be prohibited

The Jones Institute for Reproductive Medicine in Virginia, USA, created uproar in July 2001 when they published a study in the journal *Fertility and Sterility* using ES cells derived from eggs and sperms created and donated specifically for research. To compound the issue, the 12 egg donors were paid US$1500 to 2000 each, and the sperm donors US$50 each. Ironically, as no federal funds were used, no laws or regulations were violated as the US guidelines are restricted only to federally funded research, though privately funded research is urged to voluntarily comply with the safeguards and standards proposed by the US National Bioethics Advisory Committee, which opposes derivation or use of human ES cells from embryos made solely for research purposes. In our opinion, allowing the making embryos for research will lead to embryos being treated as products or as mere objects, risk commercializing procreation, and trivialize the act of procreation. We totally agree with George Annas when he wrote in an article in *New England Journal of Medicine* in 1996 that:

> *" It is society's moral attitude toward procreation and the interests of those whose gametes are involved in making the embryos that provide the moral force behind the restriction or prohibition of the manufacture of embryos for non-procreative uses. A moral framework that reduces the matter to an exclusive focus on the intrinsic properties of embryos, ignoring the interests of those whose gametes make the embryos and the circumstances under which procreation occurs, cannot persuade, or even engage, those to whom the creation of embryos solely for research is morally suspect. Obtaining consent is not enough. A new framework — one that takes relationships seriously — is essential."*

We are not sure if this concern of ours is adequately covered, or at all, by any of our existing regulation or guidelines. If none of the existing local regulations or legislation deal specifically with this, the SMA hopes that this feedback to the BAC would receive due consideration and that explicit and clear directions can be set.

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26 November 2001

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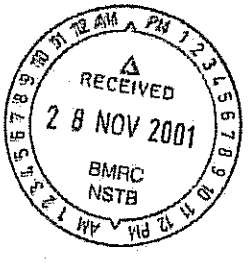
Our Ref:
SMC 14.2
Your Ref:

27 Nov 2001



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Dear Prof Lim Pin,

REQUEST FOR FEEDBACK REGARDING HUMAN STEM CELL RESEARCH IN SINGAPORE

1. I refer to your letter of 8 November 2001.

2. The Singapore Medical Council (SMC) supports in principle the overall approach of the Bioethics Advisory Committee (BAC) as stated in the consultation paper.

3. As Singapore is a multiracial, multicultural and multi-religious society, it is important that social issues in human stem cell research are accorded equal standing with ethical and legal issues.

4. Many religious bodies in Singapore believe that life begins at conception. While we foresee no fundamental ethical objections to research using adult stem cells ('AS cells'), the use of embryonic germ cells derived from aborted foetuses ('EG cells') and especially embryonic stem cells derived from early embryos ('ES cells'), even if they are not more than 14 days old, will require further deliberation by the BAC after the inputs from the various religious bodies in Singapore have been obtained.

5. The SMC supports the UK legislation and controls on embryo research which provides a degree of protection in law while allowing the benefits of any proposed research to be weighed against the respect due to the human embryo.

6. The SMC shares the views of the BAC that reproductive cloning of human beings should not be permitted while human 'therapeutic cloning', should be conducted under strict guidelines and supervision to block any potential of creating a human embryo for reproductive cloning.

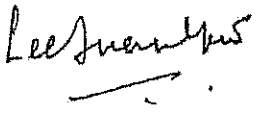
7. Although the paper has not commented on experiments on animal reproductive cloning, we feel that such experiments should be permitted for scientific purposes. It is conceivable that in the future, experiments on animal stem cells may throw light on human stem cell behaviour. The BAC is encouraged to address this issue at the outset to avoid any ambiguity in the future.

8. There is a need for Singapore to establish a system to ensure that the guidelines for stem cell research are strictly adhered to by the researchers. This may involve the setting up of a body at a national level as an oversight committee, backed by legislation that provides for stiff penalties for breaching rules governing such research.

9. The public policy balance between the opportunities that biomedical science offers to improve human welfare and the limits set by important ethical obligations will need to be regularly reviewed and redefined, where necessary, to take into account the impact of new scientific discoveries in the area of human stem cell research and changes in societal and religious mores.

10. In conclusion, I would like to thank you for inviting the SMC to share its views with the BAC on this very important issue.

Yours sincerely,



DR LEE SUAN YEW
PRESIDENT
SINGAPORE MEDICAL COUNCIL

SINGAPORE NURSES ASSOCIATION
新 加 坡 护 士 协 会
PATRON: The First Lady of the Republic of Singapore

27 December 2001

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Dear Prof Lim

The Singapore Nurses Association is pleased to be invited to give our feedback regarding Human Stem Cell Research in Singapore.

Biomedical research and development thus far has demonstrated immense potential to alleviate suffering and improve the quality of life for many with once incurable conditions. However, the threat of misuse of knowledge is real and it is wise to have in place preventive measures in the first instance. The setting up of Bioethics Advisory Committee (BAC) is indeed timely.

Nurses who have cared for couples in the fertility programmes or nursed severely premature babies in the Neonatal Intensive Care Units can particularly identify with the fragile, yet surprisingly resilient, beginnings of life. It was comforting to note that the BAC had taken much pain to give the relevant information, which addresses very real ethical and social concerns of human research.

Having some understanding of the biological properties of the human stem cells through the nursing curriculum enables nurses to understand their miraculous ability to proliferate and develop into specialised cell types. The discovery of using stem cells for new therapies, pharmaceutical development and human developmental biology holds great treatment possibilities. These new developments are especially attractive when seen in the light of the vast clinical application. The rewarding joy of being able to nurse a terminally ill patient back to health would always be a wonderful experience. It would make all the difference for the many families involved.

The consultative approach adopted by BAC to seek the views of the representative groups in the preparation of final recommendations to the Cabinet is commendable. As nurses are in direct involvement with patients and their significant others, it is very much appreciated that our views be sought in this issue. Many patients are able to confide their fears and apprehension, in the nurses caring for them. Often, we share our patients', and that of their loved ones' eager anticipation of a breakthrough which could bring hope of new cures for their debilitating and fatal illnesses. While we are members of the medical team, it is important we are able to maintain an objective perspective of contentious experimental treatment modalities.

SNA HOUSE, 77 MAUDE ROAD, SINGAPORE 208353. TEL: 3020770 FAX: 3027877
EMAIL: snaf@pacific.net.sg WEBSITE: www.sna.org.sg

SINGAPORE NURSES ASSOCIATION
新 加 坡 护 士 协 会
PATRON: The First Lady of the Republic of Singapore

The Singapore Nurses Association is confident that the BAC would continually monitor adherence to the stated recommendations and guidelines. We would appreciate if we could be kept in the loop with publications of independent review of studies, where appropriate.

Thank you.

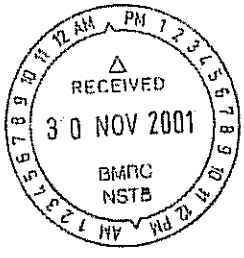
Tan Wee King
Hon Secretary
Singapore Nurses Association

SNA HOUSE, 77 MAUDE ROAD, SINGAPORE 208353. TEL: 3920770 FAX: 3927877
EMAIL: sna@pacific.net.sg WEBSITE: www.sna.org.sg

SINGAPORE NURSING BOARD

29 Nov 2001

Prof Lim Pin
Chairman
Bioethics Advisory Committee
250 North Bridge Road
#15-01/02 Raffles City Tower
Singapore 179101



Dear Prof Lim

REQUEST FOR FEEDBACK REGARDING HUMAN STEM CELL RESEARCH IN SINGAPORE

Thank you for inviting the Singapore Nursing Board to provide feedback regarding human stem cell research in Singapore.

The Board is of the view that research with AS cells and with EG cells if the decision to abort is taken separately and independently from the decision and consent to extract EG cells, would be ethically acceptable. In Singapore's society where abortions are performed on socio-economic grounds, the issue of using early embryos not more than 14 days old for serious research to benefit others, does not appear to be so ethically contentious.

We agree that reproductive cloning can be exploited and hence should be forbidden

We would like to make a few suggestions to the paper:

(1) Para 1, page 2 – ".... and adult stem cells derive from tissues such as the bone marrow, umbilical cord blood and brain..."

Perhaps placenta could be included.

Level 4, Institute of Health, 3 Second Hospital Avenue, Singapore 168937 Tel: 2361996 Fax: 2361998

(2) Under the heading "Ethical and Social Considerations"

It may be necessary to include a statement specifying that any information that could lead to the identification of donors of foetal tissue must be removed prior to the derivation or use of ES or EG cells.

We would like to commend the BAC for this succinct and well-written paper.

Yours sincerely

ANG BENG CHOO
REGISTRAR

D. SCIENTIST/RESEARCHER GROUPS

1. Biomedical Engineering Society (Singapore)
2. Science Teachers Association of Singapore
3. Singapore National Academy of Science
4. Singapore Society for Biochemical and Molecular Biology

Biomedical Engineering Society (Singapore)
c/o Orthopaedic Diagnostic Centre, National University Hospital
Lower Kent Ridge Road, Singapore 119074
Tel: 772 4424 Fax: 774 4082
Email : secretary@bes.org.sg http://www.bes.org.sg

28 November 2001

Prof. Lim Pin
Chairman
Bioethics Advisory Committee
250 North Bridge Road
#15-01/02 Raffles City Tower
Singapore 179101

Dear Prof. Lim

FEEDBACK ON HUMAN STEM CELL RESEARCH IN SINGAPORE

Thank you very much for your letter dated 8 November 2001 seeking feedback from the Biomedical Engineering Society (BES) on your Committee's current views on human stem cell research in Singapore.

The Executive Committee of BES deliberated on the consultation paper prepared by your Human Stem Cell Research Subcommittee (HSR) recently. We are in full agreement with the views expressed in the paper. We believe that they represent the best compromise between ethical concerns and the advancement of scientific research for the benefits of mankind.

Concerning your view that there must be a well-established and effective framework for the control of research involving embryos in Singapore, we would like to add further that a Registration of Researchers in this area be set up to regulate the practice of research. This can be established along the same line as that for medical doctors, professional engineers and architects, etc.

If your Committee needs further help from BES, we would be most happy to oblige.

Yours Sincerely

Prof. Chew Yong Tian
President
Biomedical Engineering Society (Singapore)

Reply to BAC from Science Teachers Association of Singapore

(STAS)

Catherine WOON/MOE/SINGOV
12-12-01 06:56 PM

To:
cc:
Subject: Re: Request for Feedback regarding human stem cell research in Singapore -please reply by 27 November 2001

---- Forwarded by Catherine WOON/MOE/SINGOV on 12-12-01 07:02 PM ----

Catherine WOON/MOE/SINGOV
26-11-01 09:15 PM

To: "Subramaniam s/o RAMANATHAN (STE)" <subrar@nie.edu.sg>@SMTP
cc: <chew@scl-ctr.edu.sg@SMTP,>
Subject: Re: Request for Feedback regarding human stem cell research in Singapore -please reply by 27 November 2001

Dr Subra and Dr Chew

I am pleased to give my views on this :

I strongly agree that there must be strict control of research involving embryos in Singapore and thus "therapeutic cloning" should only be permitted under strict conditions, only for the purpose of controlling diseases. There should be watch-dog for monitoring such research at all times. If strict control is not possible, then such research should not be carried out.

Human embryos of less than 14 days old (ES cells) created through in-vitro fertilisation techniques but not used in assisted reproduction treatments can be used for research under stringent guidelines and monitoring, again for the sole purpose of curing diseases.

I do not agree with the 1990 Act (UK) which allows the creation and use of human embryos up to 14 days old for research purposes as this, to me, goes against the natural law of procreation. Any embryo to be used for research should only come from the consent of the individual donors.

Research using AS cells should not present any ethical objections. For EG cells, I agree that no ethical issues arise from the use of such cells, so long as the decision taken to abort is taken separately and independently from the decision and consent to extract the EG cells from the foetus.

The objectives of human stem cell research must be defined very clearly to protect human life and also to prevent abuse of embryos before such research is allowed. Researchers should also be subject to the law if infringements to the stipulated guidelines drawn up are not followed.

"Subramaniam s/o RAMANATHAN (STE)" <subrar@nie.edu.sg>

"Subramaniam s/o RAMANATHAN (STE)" <subrar@nie.edu.sg>
20-11-01 03:38 PM

To: "Carmee Lim (E-mail)" <carmee@singapore.com>, Catherine WOON/MOE/SINGOV@SINGOV, "Chew Tuan Chiong (E-mail)" <chew@scl-ctr.edu.sg>, "Ohla Woon Kim (E-mail)" <woonkim@cbn.com.sg>, George GOH/MOE/SINGOV@SINGOV, "Heng Chye Kiou (E-mail)" <chyekiou@vicom.com.sg>, "Koh Lip Lin (E-mail)" <liplin@pacific.net.sg>, "LEE Peng Yee (MME)" <pylee@nie.edu.sg>, "TAN Wee Hin Leo (Director - NIE)" <whltan@nie.edu.sg>, Chye Tin LIM/MOE/SINGOV@SINGOV, "Ng Kok Lip (E-mail)" <nkl@pacific.net.sg>, Yap Kwang TAN/MOE/SINGOV@SINGOV, "Tham Seong Chee (E-mail)" <sctham@pacific.net.sg>
cc:
Subject: Request for Feedback regarding human stem cell research in Singapore -please reply by 27 November 2001

Dear Members,

Our Association has been approached by Prof Lim Pin, Chairman of the Bioethics Advisory Committee, for comments on "Human stem cell research in Singapore". A postion paper on this is enclosed for information.

We need to reply by the end of this month. Thus, we would appreciate it if you could scrutinise the enclosed paper and let us have your feedback by 27 November 2001. This would allow us some time to consolidate your inputs before reverting to the Bioethics Advisory Committee.

Responses can be sent to Dr Chew.

Thank you for your assistance.

Best wishes.
Subra

BAC.HSR. ConsultationPaper.Nov

SINGAPORE NATIONAL ACADEMY OF SCIENCE
c/o Singapore Science Centre
15 Science Centre Road
Singapore 609081
Tel : (65) 425 2500
Fax : (65) 565 9533

PATRON

Dr Toh Chin Chye

CONSTITUENT MEMBERS

Institute of Physics Singapore (IPS)

Science Teachers Association of Singapore (STAS)

Singapore Association for the Advancement of Science (SAAS)

Singapore Institute of Biology (SI Biol)

Singapore Mathematical Society (SMS)

Singapore National Institute of Chemistry (SNIC)

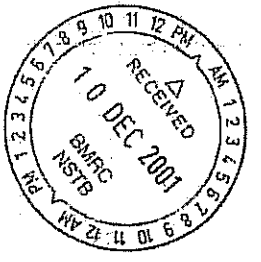
Singapore Institute of Statistics (SIS)

Singapore Society for Microbiology & Biotechnology (SSMB)

Singapore Society for Biochemistry & Molecular Biology (SSBMB)

3 Dec 2001

Professor Lim Pin
Chairman
Bioethics Advisory Committee
250 North Bridge Road
#15-01/02 Raffles City Tower
Singapore 179101



Dear Professor Lim

REQUEST FOR FEEDBACK REGARDING HUMAN STEM CELL RESEARCH IN SINGAPORE

Thank you for your letter of 12 Nov.

We have solicited feedback on the contents of the consultation paper in relation to the above from our members, and summarize herewith the comments received.

We feel that the Bioethical Advisory Committee (BAC) has taken a moderate stand with regards to the control and supervision of research on stem cells. This is a good move since any additional unnecessary imposition of restrictions compared to the existing standards elsewhere will dampen the research interest in this potential field in Singapore. As existing standards already cover the ethical issues on both adult stem (AS) cells and embryonic germ (EG) and embryonic stem (ES) cells, the committee has correctly decided not to impose special restrictions nor ethical objections to such research, provided the use of embryos is less than 14 days old as stipulated in the UK guidelines. We should also support the need for the additional mechanisms in which the BAC can review existing guidelines and policies on stem cell research on a regular basis.

Notwithstanding the foregoing, it is necessary that there be strict control of research involving embryos in Singapore, and thus "therapeutic cloning" should only be permitted under strict conditions, only for the purpose of controlling diseases. There should be a watchdog for monitoring such research at all times. If strict control is not possible, then such research should not be carried out as ethical issues will then need to be addressed.

to abort is taken separately and independently from the decision and consent to extract the EG cells from the foetus.

The objectives of human stem cell research must be defined very clearly to protect human life and also to prevent abuse of embryos before such research is allowed. Researchers should also be subject to the law if infringements to the stipulated guidelines drawn up are not followed.

Thank you and best wishes.

Yours sincerely

Professor Leo Tan Wee Hin
President

SINGAPORE SOCIETY FOR BIOCHEMISTRY
AND MOLECULAR BIOLOGY
C/O DEPARTMENT OF BIOCHEMISTRY, NATIONAL UNIVERSITY OF SINGAPORE
10 KENT RIDGE CRESCENT, SINGAPORE ~~0511~~ 119260
FAX: (65) 7791453

December 3, 2001

Professor Lim Pin
Chairman
Bioethics Advisory Committee
250 North Bridge Road
#15-01/02 Raffles City Tower
Singapore 179101.

Dear Professor Lim,

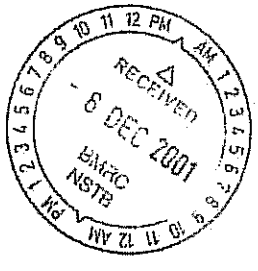
Thank you for your invitation to give our views on the BAC's consultation paper on human stem cell research. I am sorry that this reply is late.

The Council members of the Singapore Society for Biochemistry and Molecular Biology considered the document carefully. We agree with all the views expressed and believe strongly that there should be control of research involving embryos. We are concerned that the mechanisms that are put in place should be rigorous and seen to be rigorous. Because the scientific community in Singapore is very small, care must be taken such that there should not be any conflict of interests arising from membership of the appropriate governmental oversight committees which will be tasked to monitor that such research is adhering to ethical guidelines and standards.

Yours sincerely,

Hoon Eng

Dr. Khoo Hoon Eng
President
Singapore Society for Biochemistry and Molecular Biology
C/o Department of Biochemistry, Faculty of Medicine
National University of Singapore
10 Kent Ridge Crescent
Singapore 119260.



E. OTHER

1. Personal View from a Member, Inter-Religious Organisation (IRO)

INTER-RELIGIOUS ORGANISATION, SINGAPORE
(Established 1949)
Registered Address: 132 A Changi Road, Singapore 419719
Mailing Address: Raffles City P O Box 712, Singapore 911724

HINDU JEWISH ZOROASTRIAN BUDDHIST TAOIST CHRISTIAN MUSLIM SIKH BAHA'I

Tel: 383 3752, Fax 383 3753 HP 9697 9625

30 Nov 2001

Prof Lim Pin
Chairman
Bioethics Advisory Committee
250 North Bridge Road
#15-01/02 Raffles City Tower
Singapore 179101

Dear Sir

I am to refer to your letter of 8 November 2001 addressed to our President requesting feedback regarding human stem cell research in Singapore.

Attached hereto is the personal view of [redacted] an IRO Council Member, Address: [redacted] on the subject for your Committee's consideration.

Yours sincerely

HARBANS SINGH PS
Secretary

IRO2001.BACReturn

To: P Harbans Singh

Council Feedback (BAC Request)

This is my individual view not my faith's view.

(1) The problem arises with one of the 10 commandments. "Thou shalt not kill." To Christians this means human beings although an exception is made for war.

(2) A woman should not kill an unborn child since it is a separate human individual.

(3) When does a separate individual arrive? At conception or much later. I would say much later.

(4) Early embryos have no neural streak or presumably no sensation. It is therefore allowable to use the stem cells for research especially to alleviate human suffering.

(5) Such cells must be disposed of before 14 days old.

(sd) [redacted] 21/11/2001

CSGB2001.BAC(2)[redacted]

Please note that the identity of the writer has been removed in the interest of privacy.

ANNEX H

BAC DIALOGUE SESSIONS – ORGANISATIONS THAT ATTENDED

First dialogue session held on 27 December 2001

#	Organisation	Representative(s)
1	The Catholic Medical Guild of Singapore	Dr Gabriel Oon Dr John Hui (unofficially)
2	Hindu Endowments Board	Mr S. Ramesh
3	Singapore Council of Christian Churches	Dr Lee Soon Tai
4	St Anthony's Canossian Convent	Dr John Lee Hew Mun
5	Taoist Federation (Singapore)	Mr Gee Yoke Jiau
6	Majlis Ugama Islam Singapura (MUIS) (Islamic Religious Council of Singapore)	Mr Mohd Murat Mohd Aris Dr Albakri Ahmad
7	National Council of Churches of Singapore	Reverend Dr Roland Chia

Second dialogue session held on 3 January 2002

#	Organisation	Representative(s)
1	Children's Cancer Foundation	Dr Tan Hiang Khoon
2	College of Family Physicians Singapore	Dr Tan See Leng
3	Inter-Religious Organisation, Singapore	Mr Harbans Singh
4	Science Teachers Association of Singapore	Mrs Catherine Seah
5	Singapore Cancer Society	Dr Win Khin Khin
6	Biomedical Research & Experimental Therapeutics Society of Singapore	A/Prof Shabbir Moochhala
7	Singapore Nursing Board	Ms Ang Beng Choo

Third dialogue session held on 7 January 2002

#	Organisation	Representative(s)
1	Law Reform Committee, Singapore Academy of Law	Ms May Loh
2	Endocrine and Metabolic Society of Singapore	Dr Daphne Khoo
3	Singapore Dental Association	Dr Lewis Lee
4	Singapore Hospice Council	Mr Gerard Ee
5	Singapore Medical Council	Dr Tan Chi Chiu
6	The Law Society of Singapore	Mrs Murgiana Haq
7	Singapore National Heart Association	Dr C Sivathasan

ANNEX I

REPORT BY THE FEEDBACK UNIT, MINISTRY OF COMMUNITY DEVELOPMENT AND SPORTS ON THE DIALOGUE SESSION ON ES CELL RESEARCH 8 DECEMBER 2001, 10.00 AM AT ORCHARD HOTEL

Present : **Chairpersons**

Mr S Iswaran	Member, Feedback Supervisory Panel and MP for West Coast GRC
Dr Jennifer Lee	Member, Feedback Supervisory Panel and CEO, Kandang Kerbau Womens' and Children's Hospital

Presenters

Prof Ariff Bongso	Research Professor and Scientific Director, Assisted Reproductive Technology Programme, Dept of Obstetrics and Gynaecology, NUH
A/Prof John Elliott	Member, Bioethics Advisory Committee

Participants

39 participants from all walks of life, including doctors, teachers, businessmen, lawyers, architects and undergraduates.

PRESENTATIONS

1 The dialogue session was preceded by two presentations: one by Prof Ariff Bongso on the science of embryonic stem cell research, and the other by A/P John Elliott on the social and ethnic issues associated with embryonic stem cell research.

DIALOGUE SESSION

2 The dialogue session was co-chaired by Mr S Iswaran and Dr Jennifer Lee, with A/P John Elliott on the panel. The views of the dialogue participants focused on the use of embryos for research, guidelines for ES cell research, reproductive cloning, regulations on human stem cell research, role of the Bioethics Advisory Committee and public education.

USE OF EMBRYOS FOR RESEARCH

3 (Consultant Architect & Planner) said that he was "neutral" on the embryonic stem cell research as he felt that research was "ethics-blind". While he felt that the research could better equip future generations to cope with challenges in life, he warned that it could also create a "nightmare" if it was not properly handled.

4 (Undergraduate) stated that she was for the research to go on but stressed that it must be accompanied by stringent regulations to ensure that there were no abuses, and that the researchers were doing it in a responsible way.

5 (President, Investment Group) commented that the research would be acceptable if it was meant to seek cures for major illnesses such as cancer. However, it would become controversial should it be used for minor afflictions such as treatment of hair loss. AP Elliott said that in the hierarchy of possible benefits of the research, hair loss was far down the line.

6 (Medical doctor) opined that human life began at conception. She viewed ES cells as a potential human being. She was concerned that the use of the embryos for research could lead to a dangerous road to fascist thinking, if we held the belief that some lives were valued less than others. She advocated for the use of adult stem cells in place of the embryonic stem cells, as she noted that there had been successful experiments done on mice with AS cells and there were studies at Harvard that treated thalassaemia and diabetes. She hoped that more research could be done on AS cells.

7 (Doctor) shared his experience in research on AS cells. He described working with AS cells as an adult working with an abridged version of a children's story book. On the other hand, working with ES cells would be like working with the full text. He reiterated the greater potential and promise in the ES cell research. He noted that AS cells could only grow into certain kinds of tissues, while ES cells could develop into any kind of tissue and scientists believed they could make more advances using ES cells. In addition, ES cells were being used for testing of drugs for toxicity. New drugs which were currently given to very ill patients could be tested on ES cells. He recommended that researchers be allowed to work with ES cells before going on to AS cells.

8 (Doctor) felt that the trend towards the ES cell research was inevitable. If Singapore were to decide to outlaw the ES cell research, other countries like Indonesia or the US would continue with the research. If they eventually find a cure for major diseases like diabetes, would Singapore patients feel that they have been denied of the cure as a result of the law?

9 (Private Secretary) delivered a biblical story to advance his point that an embryo had a soul from the point of conception and hence should not be used for research.

10 (CEO) hoped that the ES cell research would help to prolong human life. He did not see any ethical objection to the use of excess cells, as they would be discarded anyway.

11 (Education Consultant) agreed with the need for ES cell research as he felt that it was pro-life and would improve life. He did not think that the research should be stopped just because of "the moot point that a cell is a life".

12 (Architect) felt that the 72 cell lines that was currently available from all over the world were insufficient, and that more centres and cell lines should be developed in order to benefit more people.

GUIDELINES FOR ES CELL RESEARCH

13 (Manager) felt that it was not ethical for the research to be commercialised. He opined that the research should be publicly funded and the findings should be used to benefit the masses.

14 (Accountant) asked whether the 14-day cut-off time was a given. AP Elliott said that the 14-day cut off guideline was the benchmark used. Prior to 14 days, the nervous system of the embryo has not yet developed, and would hence feel no pain. Extraction and use of ES cells occurs at day 4 or 5. (Doctor) remarked that in the US, the guidelines stated the use of ES cells before 32 days, instead of 14 days.

15 (Lawyer) felt that the reason he had difficulty with the 14-day cut off time was the rationale to justify the use of the cells. He felt that the crux of the issue was whether there is life in the cells or not, regardless of how mature they are. He asked whether it was morally right to experiment with a cell prior to 14 days just because it does not feel pain. Following this argument, he asked if one thought that a comatose patient was less human than a healthy person since he could not feel pain.

16 (Managing Director) asked whether a patient would be informed before he was given treatment using stem cells. Second, he wondered whether persons undergoing stem cell treatment would be made to disclose this fact to insurance companies.

17 (Theatre Director) stressed that research subjects should be fully informed of the full implications in order for them to "make educated choices". He added that while the issue of transparency in research was important, there was a need to ensure accountability.

18 (Undergraduate) asked whether IVF patients were told about the fate of their excess embryos at the early stages of their treatment or was the choice to donate their cells for research came only after they had completed their treatment. Mr Iswaran noted her point that there would have to be, in principle, a difference between the decision for a couple to undergo IVF, and

the decision to donate excess embryos for research. In other words, there must be a de-coupling of the decision process and medical research personnel involved in these two stages to avoid any conflict of interest.

19 (Undergraduate) queried about the resource allocation of such treatment should it be successful. AP Elliott pointed out that the issue of resource allocation in medical treatment was not unique or particular only to treatment of disease by ES cells.

20 (Teacher) stressed the importance of knowing the source of the embryos. He also expressed concern that parthenogenesis could lead to women donating their eggs in exchange for money. He stressed that the aim of the research should not be profit-driven, but rather for the good of mankind.

21 (Merchant) said that he was concerned that the public was only hearing the positive side of the issue. He wondered what could be the consequences if human errors occur. AP Elliott commented that scientific research was a transparent process. It was not possible for researchers to hide any negative points as findings from reputable research institutions were made public.

REPRODUCTIVE CLONING

22 (Mr) said that he personally preferred the use of excess embryos from IVF procedures for research to those from therapeutic cloning, which was too close to the slippery slope of reproductive cloning.

23 (Lawyer) said that he was against reproductive cloning. But he was concerned that if ES cell research were to be allowed, one would argue why therapeutic cloning and reproductive cloning could not be allowed. He also commented that this was the "same ethic with the Nazi experiment". (Education Consultant), however, felt that there was a need to move on and not be "so sensitive".

24 (Mr) asserted that should the BAC take the stand on no funding for reproductive cloning, it should not "go by the back door" and fund this research elsewhere either.

25 (Managing Director) felt that therapeutic cloning was alright but it should not move on to reproductive cloning.

REGULATIONS ON HUMAN STEM CELL RESEARCH

26 (Architect) felt that there was a need to have a regulatory body in Singapore. He pondered, however, how we could go about regulating researchers who conduct their research privately.

27 (Mr) was also concerned with control of technology and felt that there was a need to control underground research work.

28 (CEO) felt that there would be difficulties in controlling the research. He pointed out that while companies dealing with drugs such as heroin were required to maintain accounts of storage and movement of these substances, heroin continued to be manufactured and circulated illegally. He felt that we should be realistic about how much we could control the human stem cell research.

29 (Doctor) opined that even with the best of regulations, enforcement of regulations was difficult. The situation might develop into a state where we have stockpiles of therapeutic clones and this would become a nightmare in disposing them. She also felt that there could be incompatibility and rejection of tissues by recipients.

30 (Doctor) felt that it was important that the government support ES cell research with public funds. He said that the furore in the US over President George Bush's recent announcement was that all the US government did was to limit public funding, which resulted in a flight of top talents to private companies. As long as the research is public funded, the process would remain transparent and could be easily regulated. Private funded research would be more interested in obtaining patents to make profits and would be difficult to track.

ROLE OF BAC

31 (Doctor) commented that he had heard a lot about the BAC but wondered what mechanisms were to take place, and had any regulations been put in place. AP Elliott clarified that the BAC was an advisory body tasked to examine the issues pertaining to the research held in Singapore and it would make recommendations to the Life Sciences Ministerial Committee.

32 (Undergraduate) asked what would happen if there was disagreement on the human cell research. Mr Iswaran clarified that the objective of the session was to find out the tolerable limit among the public. If the research in embryos within 14 days was acceptable and should go on, then the next step was to ensure that this was done in a responsible manner, followed by the stipulations of the consequences of transgressions.

33 (Head of Department) pondered whether, given that Singapore had already committed itself to the pursuit of the life sciences, research into ES cells was a given. Mr Iswaran said that research into ES cells was just but one facet of research in the life sciences, and that the BAC's position was still open.

34 (Teacher) said that as research was already going on, would the purpose of this discussion be on whether the research into such technology should go on or not, or rather regulatory issues for a field which had yet to be regulated in

Singapore. It was pointed out that the Singapore team of researchers in this field had been commended by the international research community as being very stringent in their adherence to regulations. As far as the BAC was concerned, it would advise the Government on the ethical issues and whether more regulations were needed.

PUBLIC EDUCATION

35 (Engineer) commented that Professor Bongso had delivered a good presentation which cleared a lot of misconceptions. But he felt that the general public also needed to be educated on this issue. He agreed with the BAC's position that specific religious stands should not be allowed to influence the policy. Otherwise, we would also need to rethink our laws on other issues like abortion and death penalty. (Mr) also agreed that BAC should not allow any religious viewpoints to dominate this debate.

36 (Retiree) stated that he was against ES cell research, despite, with tongue-in-cheek, that he stood to benefit from a hair loss cure. He hoped that there could be another session for the Chinese-educated, as they also needed to be educated on the issue and be given the opportunity to provide feedback. Their perspective could be different from that of the English-speaking group.

37 (Principal, Primary School) shared that children's discourse on the matter were more pertaining to the uses of the research instead of the way the research is conducted. She pointed out that her students had painted a scenario where a society would be full of old people as people don't die, and no EM3 students as genes could be modified. Hence, she felt that children should be educated on the ethics of the bio-research while schools were giving more emphasis on life sciences.

CONCLUSION

38 Mr Iswaran thanked the participants on behalf of the BAC and the Feedback Unit for their frank feedback. He said that their views would be channeled to the relevant agencies for their consideration. The session ended at 1.25 pm, followed by a briefing to the media by the chairpersons.

Drafted by : Suhaila Binte Ahmad
Executive Officer, Feedback Unit

Teo Chor Heng, Allison
Asst Head, Feedback Unit

Vetted by : Mr Shee Poon Kwee
Deputy Head, Feedback Unit

Approved by : Mr S Iswaran
Member, Feedback Supervisory Panel

Dr Jennifer Lee
Member, Feedback Supervisory Panel

Date : 11 December 2001

* Please note that individual names in the above noted dialogue session have been removed in the interest of privacy.

ANNEX J

PERSPECTIVES AND POSITIONS ADOPTED BY COUNTRIES WORLDWIDE

Country/ Group	Reproductive Cloning	Therapeutic Cloning	Embryonic research	Stem cell research	Remarks
Austria	Banned	Banned	Banned	No guidelines to date	Creation of embryos for reproductive purposes only (Law No. 275 of 1992 on reproductive medicine).
Australia	Banned	Banned 3 year moratorium on the creation of embryos via SCNT. Research has not identified any specific opportunities warranting such creation.	Allowed Use of surplus embryos (from infertility treatments) subject to approval by international ethics committee, national licensing body and strict adherence to guidelines. The deliberate creation of embryos for research purposes is prohibited.	Allowed	Human cloning banned till adoption of uniform laws under the Federal Gene Technology Act. No other guidelines except bans in three states on human cloning research[1]. Position tabled in the House of Representatives, 17 September 2001[2]. Use of surplus embryos (from infertility treatments) subject to approval by international ethics committee, national licensing body and strict adherence to guidelines. The deliberate creation of embryos for research purposes is prohibited
Belgium	No guidelines to date	No guidelines to date	Draft bill allows research involving surplus embryos	Allowed	Draft bill prohibiting production of embryos for research purposes, with many exceptions.
Brazil	Banned	Banned	Banned	No guidelines to date	Law No. 8974/95 on genetic engineering prohibits production, storage and manipulation of human embryos for use as biological material.
Canada	No guidelines to date	No guidelines to date	Allowed Research using surplus embryos permitted, subject to donor consent.	Allowed	Guidelines already drafted and sent to a committee for consideration and public consideration. Wide restrictions on research and ban on cloning expected[3].
Costa Rica	Banned	Banned	Banned	No guidelines to date	Right to life recognised from moment of conception (Law No. 7739 of 1998).

Country/ Group	Reproductive Cloning	Therapeutic Cloning	Embryonic research	Stem cell research	Remarks
Ecuador	Banned	Banned	Banned	No guidelines to date	Right to life recognised from moment of conception (Art. 49, par. 1, of the Constitution (1998).
France	Banned	Banned	Banned	Allowed	Banned all research on cloning and severely restricts research on frozen embryos[4]. Position currently under review.
Finland	No guidelines to date	No guidelines to date	Allowed	Allowed	Research using surplus embryos permitted, subject to donor's consent. (Law No. 115).
Germany	Banned	Banned	Banned	Allowed	Creation of embryos for reproductive purposes only (Law of 13 December 1990 on Embryo Protection). Relaxation of rules sought by scientists[5].
Hungary	Banned	Banned	Banned	No guidelines to date	Life of unborn child must be protected at conception (Law No. LXXIX of 1992).
Ireland	Banned	Banned	Banned	No guidelines to date	Article 40, paragraph 3 of the Constitution expressly prohibits research on embryos. Right to life of unborn child is equal to that of the mother.
Israel	Banned	No guidelines to date	Allowed	Allowed	The Prohibition of Genetic Intervention Law (Cloning Human Being and Genetic Modifications of Reproductive Cells) bans reproductive cloning for a period of 5 years from 1999. No legislation regulating stem cell research.
Italy	Banned	Banned	Banned	Allowed	Specifically prohibits creation of embryos for research purposes and early splitting of embryos for therapeutic or research purposes. Italian National Committee on Bioethics opposes reproductive cloning (Opinion of 27 October 2000). Government under pressure from both Vatican and scientists[6].
Japan	Banned	Allowed	Allowed	Allowed	Human Cloning Regulation Act enacted on 30 November 2000, bans implantation of embryos created for research into the woman's womb. Guidelines on human stem cell research pending.

Country/ Group	Reproductive Cloning	Therapeutic Cloning	Embryonic research	Stem cell research	Remarks
Nether-lands	No guidelines to date	No guidelines to date	Draft bill allows research involving Surplus embryos	No research to date	Draft bill prohibiting production of embryos for research purposes, with many exceptions.
Norway	Banned	Banned	Banned	No guidelines to date	Creation of embryos for reproductive purposes only (Law No 56 of 5 August 1994).
Peru	Banned	Banned	Banned	Allowed	Prohibits human cloning and fertilisation of human ova for purposes other than reproduction (Law No. 26.842). Right to life recognised from moment of conception (Law No.27.337).
Poland	Banned	Banned	Banned	No guidelines to date	Life of unborn child must be protected at conception (Law of 7 January 1993, amended 30 August 1996)
Spain	Banned	Banned	Permitted for surplus embryos	Allowed	Permitted for surplus embryos. Creation of embryos for research purposes prohibited (Law No. 35/1988). Observatory of Law and Bioethics expressed its support for the creation of embryos for research purposes, by donation and by cloning techniques (September 2000).
South Korea	No guidelines to date	No guidelines to date	No guidelines to date	No guidelines to date	New guidelines expected at end of 2001. Draft bill announced by Science Ministry bans all embryo creation except for infertility treatments[7].
Sweden	Banned	Banned	Allowed	Allowed	Research using surplus embryos permitted, subject to donor's consent and if no acceptable alternative exists. (Law No. 1991:115 and Law No. 1982:763)
Switzerland	Banned	Banned	Banned	No guidelines to date	Constitution prohibits medically assisted reproductive cloning for research purposes (Art. 19, 2c)
Tunisia	Banned	Banned	Banned	No guidelines to date	National Medical Ethics Committee opposes all experimentation on the embryo, which is regarded as a "potential person" (Opinion No. 1 of 12 December 1996) and opposes any form of cloning (Opinion No. 3 of 22 May 1997)

Country/ Group	Reproductive Cloning	Therapeutic Cloning	Embryonic research	Stem cell research	Remarks
UK	Not banned by the 1990 Act, but no license will be issued by the HFEA	Allowed	Allowed	Allowed	Human stem cell research regulated by the Human Fertilisation and Embryology Act 1990, Human Tissue Act 1961 and the Code of Practice on the Use of Fetuses and Fetal Material in Research and Treatment 1989.
US	Banned	Banned	Only existing stem cell lines	Allowed	Applies to research using federal funds. No restriction for research projects using private funds.
American Convention Human Rights of 1969					Art. 4 stipulates that "every person has the right to have his life respected. This right shall be protected by law and, in general, from the moment of conception". Twenty six countries have ratified the Convention: Argentina, Barbados, Bolivia, Brazil, Chile, Colombia, Costa Rica, Dominica (Commonwealth), Dominical Republican, Ecuador, El Salvador, Grenada, Guatemala, Haiti, Honduras, Jamaica, Mexico, Nicaragua, Panama, Paraguay, Peru, Suriname, Trinidad and Tobago, United States of America, Uruguay and Venezuela.
Council of Europe's Convention for the Protection of Human Rights and Dignity of the Human Being					Application of Biology and Medicine of 1997 stipulates a prohibition of creating embryos for research purposes and the provision of adequate protection of the embryo. Seven countries have ratified the Convention: Denmark, Greece, San Marino, Slovakia, Slovenia, Spain and Sweden. An additional protocol to the Convention on the Prohibition of Cloning Human Beings approved in 1998, and took effect on 3 January 2001 in these countries: Georgia, Greece, Slovakia, Slovenia and Spain.

[1] Herald Sun – June 1, 2001.
[2] "Human cloning: Scientific, ethical and regulatory aspects of human cloning", presented by the Standing Committee on Legal and Constitutional Affairs and tabled in the House of Representatives, 17 September 2001.
[3] CBC News – Ottawa delivers rules on reproductive cloning – May 4, 2001.
[4] CNN.com – France forbids human cloning – June 20, 2001.
[5] Asian Wall Street Journal – May 31, 2001; www.cnn.com – Archbishop condemns embryo research – December 20, 2000.
[6] CNN.com – Clash over Italy gene research – February 13, 2001.
[7] Joins.com – May 25, 2001.

GLOSSARY OF TERMS

adult stem (AS) cells – stem cells derived from certain adult tissues (such as bone marrow, brain, skin, intestine, and blood cells of the umbilical cord at the time of birth). They are more differentiated than embryonic stem cells or embryonic germ cells.

assisted reproductive technology (ART) – all treatments or procedures that involve the handling of human eggs and sperm for the purpose of helping a woman become pregnant. Types of ART include *in vitro* fertilisation, gamete intrafallopian transfer, zygote intrafallopian transfer, embryo cryopreservation, egg or embryo donation, and surrogate birth.

blastocyst – a preimplantation embryo of 30-150 cells. The blastocyst consists of a sphere made up of an outer layer of cells (the trophectoderm), a fluid filled cavity (the blastocoel), and a cluster of cells on the interior (the inner cell mass).

bone marrow – the soft, living tissue that fills most bone cavities and contains hematopoietic stem cells, from which all red and white blood cells evolve. The bone marrow also contains mesenchymal stem cells that a number of cells types come from, including chondrocytes, which produce cartilage.

cadaveric – of, pertaining to, or resembling, a corpse, or the changes produced by death; cadaverous; as, cadaveric rigidity.

chromosomes – nucleic acid-protein structures in the nucleus of a cell. Chromosomes are composed chiefly of DNA, the carrier of hereditary information. Chromosomes contain genes, working subunits of DNA that carry the genetic code for specific proteins, interspersed with large amounts of DNA of unknown function. A normal human body cell contains 46 chromosomes; a normal human gamete, 23 chromosomes.

clones – two or more organisms that have exactly the same DNA. Identical twins are naturally occuring human clones.

cloning – the production of an exact genetic copy of all the genetic material in a molecule (including DNA), cell, tissue, plant, animal, or human.

cloning technology – linked with human stem cell research. A distinction between reproductive cloning and therapeutic cloning is drawn. (See reproductive cloning and therapeutic cloning).

differentiation – the specialisation of characteristics or functions of cell types.

DNA – Deoxyribonucleic acid, a chemical found primarily in the nucleus of cells. DNA carries the instructions for making all the structures and materials the body needs to function.

embryo – the beginning of any organism in the early stages of development; a stage (between the ovum and the foetus) in the prenatal development of a mammal.

embryonic germ (EG) cells – stem cells which originate from primordial reproductive cells of developing foetuses, and can be derived from cadaveric foetal tissues.

embryonic stem (ES) cells – stem cells which originate from early human embryos and may be obtained from human embryos created by in vitro fertilisation (IVF), by cloning techniques, or from existing embryonic stem cells lines. ES cells are primitive (undifferentiated) cells from the embryo that have the potential to become a wide variety of specialised cells.

fertilisation – the process whereby male and female gametes unite.

gene – a functional unit of heredity that is a segment of DNA located in a specific site on a chromosome. A gene directs the formation of an enzyme of other protein.

genome – the complete genetic material of an organism.

germ cells – gametes (ova and sperm) or the cells that give rise directly to gametes.

immunogenic – relating to or producing an immune response.

in utero – in the uterus.

in vitro – in an artificial environment, such as a test tube or culture medium

in vitro fertilisation (IVF) – an assisted reproduction technique in which fertilisation is accomplished outside the body.

in vivo – in the natural environment (i.e., within the body)

neural tube – the embryological forerunner of the central nervous system.

pluripotent stem cell – a single stem cell that has the capability of developing cells of all germ layers (endoderm, ectoderm, and mesoderm).

pre-implantation embryo – the embryo before it has implanted in the uterus; term commonly used to refer to *in vitro* fertilised embryos before they are transferred to a woman's uterus.

primitive streak – the initial band of cells from which the embryo beings to develop. The primitive streak establishes and reveals the embryo's head-tail and left-right orientations.

reproductive cloning – refers to the application of cloning technology to animal or human cells that result in the creation of a complete animal or human being.

somatic cell nuclear transfer (SCNT) – the transfer of a cell nucleus from a somatic cell into an egg from which the nucleus has been removed.

somatic cells – [from *soma* – the body] 1) all cells of an organism with the exception of germ cells. 2) cells of the body which in mammals and flowering plants normally are made up of two sets of chromosomes, one derived from each parent.

stem cells – unspecialised cells that are able to differentiate into a range of cell types with specialised functions. A stem cell has the ability to divide for indefinite periods in culture and to give rise to specialised cells. There are three widely recognised types of stem cells- adult stem cells, embryonic stem cells, and embryonic germ cells.

stem cell line – a colony of stem cells, taken from a single embryo, that can reproduce themselves indefinitely.

therapeutic cloning – describes the use of cloning technology on stem cells for therapeutic or research purposes that do not result in the creation of a complete animal or human being. Therapeutic cloning is believed to hold potential for furthering the understanding and treatment of human diseases.

tissue culture – growth of tissue in vitro on an artificial medium for experimental research.

totipotent – having unlimited capacity. The totipotent cells of the very early embryo have the capacity to differentiate into extra-embryonic membranes and tissues, the embryo, and all postembryonic tissue and organs.

zygote – the cell resulting from the fusion of two gametes in sexual reproduction; a fertilized egg (ovum); the diploid cell resulting from the union of a sperm and an ovum; the developing organism during the first week after fertilisation.