Report of the Independent Review

of the

Prohibition of Human Cloning for Reproduction Act 2002

and

Research Involving Human Embryos Act 2002

A Report to the Parliament and
the Council of Australian Governments

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Legislation Review Committee
Prohibition of Human Cloning for Reproduction Act 2002
and *Research Involving Human Embryos Act 2002*

27 May 2011

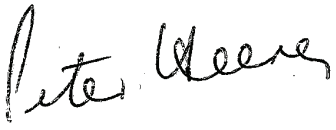
The Hon Mark Butler MP
Minister for Mental Health and Ageing
Parliament House
CANBERRA ACT 2600

Dear Minister

In accordance with sections 25A and 47A respectively of the *Prohibition of Human Cloning for Reproduction Act 2002* and the Research Involving Human Embryos Act 2002, I have the honour to present the reports of the Legislation Review Committee on the operation of these Acts.

These reports are presented to you for tabling in both Houses of Parliament and presentation to the Council of Australian Governments.

Yours sincerely



The Hon Peter Heerey QC
Chair
Legislation Review Committee

cc

The Hon Julia Gillard MP, Prime Minister
The Hon Nicola Roxon MP, Minister for Health and Ageing

1. FOREWORD

Both the *Prohibition of Human Cloning for Reproduction Act 2002 and the Research Involving Human Embryos Act 2002* were enacted in 2002. A committee chaired by the Hon John Lockhart AO QC reviewed the Acts in 2005.

Amendments in 2006 to both Acts required a further review to be undertaken three years after the Acts came into effect. In December 2010, the Minister for Mental Health and Ageing, the Hon Mark Butler MP, appointed the Legislation Review Committee (the Review Committee) to undertake the independent reviews required by Acts.

As with the 2005 review, the task set for the 2010 Legislation Review Committee has been challenging. Questions of ethics, social values, community attitudes and the need for scientific research arose.

The Review Committee received submissions from members of the public, scientific and other organisations, State Governments and the National Health and Medical Research Council (NHMRC). Details of submissions are contained in Schedule 1.

The Review Committee met with selected individuals and organisations covering a broad range of views. Details are contained in Schedule 2.

Administrative support was provided by officers from the NHMRC, Dr Timothy Dyke, Mr Mick Hoare and Ms Sarah Busby. The Review Committee is most grateful for their unfailing support.

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3. EXECUTIVE SUMMARY

3.1 Legislation and Reviews

In the 1990s, scientific advances in human embryo research and cloning prompted many countries around the world to consider the impact of this work.

In 1998, the then Minister for Health and Aged Care, Dr Michael Wooldridge MP, asked the Australian Health Ethics Committee (AHEC) to report to him on the scientific, ethical and regulatory considerations relevant to cloning of human beings.

In its report, AHEC made a number of recommendations including that the Minister should encourage informed community discussion on the potential therapeutic benefits and possible risks of the development of cloning techniques.

In 2001, the House of Representatives Standing Committee on Legal and Constitutional Affairs report – *Human Cloning: Scientific, Ethical and Regulatory Aspects of Human Cloning and Stem Cell Research*, recommended:

- the enactment of legislation to regulate human cloning and stem cell research;
- that such legislation should include a ban on cloning for reproductive purposes combined with criminal penalties and loss of an individual's research licence; and
- the establishment of a national licensing body empowered to issue licences for research involving the isolation, creating and use of embryonic stem cells.

In April 2002, at a Council of Australian Governments the Prime Minister and all Premiers and Chief Ministers agreed that the Commonwealth, States and Territories would introduce nationally consistent legislation to ban human cloning and other unacceptable practices and that research be allowed only on excess embryos from assisted reproductive technology (ART) procedures, being embryos that would otherwise have been left to expire. There was to be a strict regulatory regime, including requirements for the consent of donors.

A draft bill was prepared and after consultations undertaken by the NHMRC in each state and territory a Bill was introduced into Parliament on 27 June 2002.

The Bill was referred to the Community Affairs Legislation Committee. After extensive debate in the House and the Senate the Parliament enacted two Acts: the *Prohibition of Human Cloning Act 2002* and the *Research Involving Human Embryos Act 2002*.

As required by the two Acts, a Legislation Review Committee, chaired by the Hon John Lockhart AO QC (Lockhart Committee), was appointed in June 2005 and reported on 19 December 2005. The committee made 54 recommendations, including provisions for further review.

In 2006, following the Lockhart Committee report, amendments were made to the two Acts, including the renaming of the *Prohibition of Human Cloning Act 2002* to the *Prohibition of Human Cloning for Reproduction Act 2002*.

2010/2011 Legislation Review

Section 25A of the *Prohibition of Human Cloning for Reproduction Act 2002* and 47A of the *Research Involving Human Embryos Act 2002* contain legislative provisions for this review, which are similar to the earlier review provisions.

The reviews are to be undertaken concurrently and by the same persons. The persons undertaking the review are to be chosen by the Minister, with the agreement of each State and Territory.

The Review's Terms of Reference (ToRs) are set out in the legislation and require the persons undertaking the Review to consider and report on the scope and operation of the Acts, and make recommendations regarding amendments, if any, that should be made to the Acts, taking into account:

(a) developments in assisted reproductive technology, including technological, medical and scientific developments, and the actual or potential clinical and therapeutic applications of such research;

(b) developments in embryonic stem cell research, including technological, medical and scientific developments, and the actual or potential clinical and therapeutic applications of such research;

(c) community standards;

(d) a brief analysis of international developments and legislation relating to the use of human embryos and related research;

(e) an analysis of research resulting from the licenses granted;

(f) any National Stem Cell Centre and any national register of donated excess ART embryos;

(g) an evaluation of the effectiveness of legislative provisions and NHMRC guidelines relating to proper consent;

(h) an evaluation of the range of matters for which the NHMRC Licensing Committee may issue a licence and any recommendations to increase, decrease or alter these arising from the evaluation;

(i) an analysis of any research or clinical practice which has been prevented as a result of legislative restrictions;

(j) the extent to which the NHMRC Licensing Committee has effectively used information and education tools to assist researchers working in the field, and any ongoing need for legally binding rulings;

(k) the extent of Commonwealth/State cooperation in the area of human embryo research and the requirement for further Commonwealth or State legislation on the matter.

The persons undertaking the review must consult the Commonwealth and the States and Territories and a broad range of persons with expertise in or experience of relevant disciplines. The views of those parties must be set out in the report to the extent that it is reasonably practicable to do so.

On 21 December 2010, after consulting with State and Territory Governments, the Minister for Mental Health and Ageing, the Hon Mark Butler MP, announced the review of the two Acts and appointed an independent five person committee, listed below, chaired by the Hon Peter Heerey QC.

The Honourable Peter Heerey, QC, BA, LLB (Hons) (Tas), ACIArb

The Hon Peter Heerey QC served as a Judge of the Federal Court of Australia for over 18 years. During this time he also held appointments as President of the Australian Defence Force Discipline Appeal Tribunal, a Deputy President of the Australian Competition Tribunal, and as a Presidential Member of the Administrative Appeals Tribunal. He retired from the Court in 2009. He is currently Chairman of the Australian Electoral Commission and has returned to practice at the Victorian Bar specialising in advice, arbitration and mediation.

Professor Loane Skene, LLD (Melb), LLM (Mon), LLB (Hons) (Melb)

Professor Skene is a prominent lawyer, ethicist and academic. She has had extensive experience in relation to genetics and law. She is currently a member of the Australian Health Ethics Committee and has served on numerous federal and state advisory committees. In 2005, she was Deputy Chair of the Lockhart Committee on Human Cloning and Embryo Research and became the spokesperson for the committee in 2006 after the death of Mr Lockhart. Professor Skene is currently a Professor of Law in the Melbourne University Law School and an Adjunct Professor in the Faculty of Medicine, Dentistry and Health Services at the University of Melbourne.

Professor Ian Frazer, MBChB (Edin), FRCP (Edin), FRCPA, FAA, FTSE, FRS

Professor Frazer is a leading researcher in the field of immunology and cancer research. He was named Australian of the Year in 2006 for his research on the link between papilloma viruses and cancer and for creating of human papillomavirus vaccine against cervical cancer.

Professor Frazer holds research funding from several Australian and US funding bodies. He is a director of a biotechnology start-up company, Coridon, with an interest in optimising and targeting polynucleotide vaccine protein expression. He is chair of the scientific advisory committee of the International Agency for Cancer Research and past president of Cancer Council Australia.

Reverend Kevin McGovern, STL (Weston) DipApSc (QUT)

Reverend McGovern is a Catholic priest and is currently the Director of the Caroline Chisholm Centre for Health Ethics in East Melbourne. From 1993 to 1996, he studied ethics and moral theology at the Weston Jesuit School of Theology in Boston where he was awarded a Licentiate degree in theology. From 1997 to 2006, he lectured at the Brisbane College of Theology, where he taught courses in fundamental moral theology, sex and sexuality, marriage and family, Catholic social teaching, and bioethics.

Dr Faye Thompson, RN, EM, BA (UQ), DipApSc (Nr Ed) (QUT), MNSt (LaTrobe), PhD (USQ), FRCNA

Dr Thompson has over 20 years experience as a midwife and educator in a variety of tertiary teaching institutions. She has published extensively and is internationally recognised for identifying the ethics that are implicit in the practice of midwifery. She has been an appointed member of several national and international committees including the Queensland Government Maternity Service Steering Committee and was the lead consultant in the development of a National Code of Ethics and Code of Professional Conduct for Midwives in Australia.

3.3 Stem Cell Research

The human body is constituted by billions of cells. There are some 200 types of cells, which make up the various organs such as skin, liver etc.

Stem cells are cells which can develop into different types of cells. They can also be grown continuously in the laboratory to produce stem cell lines.

Stem cells fall into two classes, embryonic stem cells (ES cells) which exist in the embryo, and 'adult' stem cells (stem cells that are not ES cells), which can be found in the various tissues and organs of the human body. ES cells are said to be 'pluripotent', that is to say they have power to differentiate into any type of cell found in the body. Adult stem cells are somewhat less potent in this regard, and the type of cells into which they may develop is limited.

Some years ago, scientists developed the process of somatic cell nuclear transfer (SCNT). This involves taking the nucleus from an egg and replacing it with the nucleus of a somatic cell. A somatic cell is a cell from the body, other

than eggs or sperm. The use of an embryo produced by SCNT is prohibited in reproduction under s13 of the *Prohibition of Human Cloning for Reproduction Act 2002*. An embryo produced as a result of SCNT contains pluripotent ES cells.

In 2007, scientists found out how to make induced pluripotent stem cells (iPS cells) by taking an adult somatic cell and inducing it to a stem-like condition by a forced expression of certain genes. To some extent (just how much is the subject of extensive current research) iPS cells have a similar pluripotent capacity to ES cells derived from an embryo.

Research with ES cells has already shown great potential. ES cells can be used to develop *in vitro* models of diseases on which drugs may be tested. Human ES cells, probably after further development in the laboratory, may be transplanted into people with particular medical conditions to replace diseased or defective organs, tissues or cells. It is claimed that by this means, in the future, paraplegics may be able to walk again, and severely disabling conditions such as Parkinson's disease and Huntington's disease may be prevented or cured.

A particular advantage of iPS cells and SCNT derived ES cells used for organ or tissue replacement is that the derived cells, tissues or organs would be placed in the body of the provider of the genetic information for the stem cell, thus reducing the likelihood of rejection by the body's immune system and the need for lifetime treatment with immune suppressing drugs.

Research with ES cells necessitates deliberate destruction of the embryo from which they are derived. For this reason many people say that research using excess embryos from assisted reproductive technology (ART) procedures is morally and ethically wrong, since it involves the deliberate destruction of human life, albeit that the excess embryos would in any event be left to expire.

They argue that creation and use of embryos derived by SCNT is ethically even less acceptable than destruction of ART embryos because SCNT embryos are deliberately created for the purpose of destruction.

At a practical level, such objectors point to the lack of progress with SCNT cells and to the recent development of iPS cells, which are said to pose no ethical problems, and already have much of the potential for generation of pluripotent stem cells that is observed for ES cells from ART embryos, and that might be expected from SCNT derived ES cells. Therefore, they say, there is now no justification for the continued use of ES cells, and particularly of SCNT derived ES cells.

The contrary view points out that there have been significant developments from human ES cell research, although accepting that progress with SCNT cells has not lived up to the hope (and hype) which attended their discovery.

Moreover, proponents of ES cell research say that iPS cells are not a proven true equivalent of ES cells, and that more research is needed. They accept the legitimacy of ethical concerns, but say that, on balance, these are met by the current strict statutory regime that requires independent scientific and ethical approval and monitoring. They also argue that the potential for research using ES cells to lead to means of alleviating human pain and misery must be weighed in the balance.

Of the many issues and questions the Review Committee had to consider, the continued attempts to generate human embryos by SCNT was the most contentious.

Indeed the Review Committee is not unanimous in its recommendation, which is that SCNT research may continue, subject to the existing legislative and administrative controls.

3.4 Public Submissions

The opportunity to make public submissions was available via the Legislation Review Website (www.legislationreview.nhmrc.gov.au) from 15 January 2011. Submissions closed 15 March 2011. A total of 264 submissions were received compared to 1,035 during the 2005 review. Of the 264 submissions, 170 were from private individuals with 158 of the total marked as 'not for public viewing' by the submitter.

Of the total number of 264 submissions, 188 were from the general community or from non-scientific organisations; six were international and the remainder from scientists or scientific organisations. No submissions supported human cloning for reproduction. Of the submissions from individuals, 112 specifically commented that they did not support human cloning, while 188 stated that they did not support the use of human embryos for research.

3.5 Appearances

After considering written submissions, the Review Committee selected individuals and organisations and invited them to meet with the Review Committee face to face. Those invited represented a broad range of opinions including those from the ethical, scientific and religious sectors. Three scientific experts (Professor Bob Williamson, Dr Megan Munsie and Professor Sankot Marzuki) were also asked to respond to specific questions from the Review Committee.

3.6 Recommendations

The Review Committee has considered many issues. While the Review Committee has recommended some changes to the legislation, mostly concerned with enhancing the powers of the NHMRC Embryo Research Licensing Committee (established under the *Research Involving Human Embryos Act 2002*), we believe that the basic structure of the legislation introduced in 2002, as amended in 2006, should remain.

The Review Committee considers that there should continue to be a criminalisation of human cloning for reproduction, and of the other conduct specified in the *Prohibition of Human Cloning for Reproduction Act 2002*.

Research involving human embryos should only be permitted under license and with ongoing monitoring by the NHMRC Embryo Research Licensing Committee (the Licensing Committee).

Unless otherwise indicated, the Review Committee's recommendations are unanimous.

> **Recommendation 1:** Cloning of a human being for reproduction should remain a criminal offence. The other criminal offences in the *Prohibition of Human Cloning for Reproduction Act 2002* should also remain.
>
> **Recommendation 2:** (by majority) Research involving embryos and ES cells should continue to be permitted subject to the statutory controls in the present legislation.
>
> **Recommendation 3:** (by majority) The provisions in the current legislation regarding SCNT should not be amended.
>
> However, in reaching this recommendation, the Review Committee notes the lack of progress in SCNT research in animals and humans. The Review Committee believes that this must impact on the Licensing Committee's interpretation of its statutory obligation, when it is considering any future application for a licence to undertake research involving SCNT, to take into account 'the likelihood of significant advance in knowledge or improvement in technologies for treatment as a result of the use of excess ART embryos or human eggs, or the creation or use of other embryos, proposed in the application, which could not reasonably be achieved by other means' when it is considering any future application for a licence to undertake research involving SCNT.

Recommendation 4: The provisions in the current legislation regarding the cooling-off period related to the use of excess ART embryos for research should not be amended.

Recommendation 5: There should be no change to the legislation that would permit research on embryos later than the point where the egg divides into two cells (the first mitotic division).

Recommendation 6: There should be no change to s 21 of the *Prohibition of Human Cloning for Reproduction Act 2002* in relation to the payment of 'reasonable expenses'.

Recommendation 7: (by majority) There should be no change to the current legislation in relation to the use of DNA from more than two persons.

Recommendation 8: The current framework for research involving human embryos which involves ethical assessment by a Human Research Ethics Committee and assessment of applications for licenses by the Licensing Committee should continue.

Recommendation 9: In consultation with the Licensing Committee and other relevant stakeholders, AHEC and NHMRC should establish a system of credentialing for HRECs that consider research involving embryos.

Recommendation 10: Section 20(1)(d) of the *Research Involving Human Embryos Act 2002* should remain unchanged, permitting under licence the creation and use for research purposes of human embryos using precursor cells from a human embryo or a human fetus.

Recommendation 11: (by majority)**:** Section 20(1) of the *Research Involving Human Embryos Act 2002* should be amended to include that a person may apply to the NHMRC Licensing Committee for a licence authorising the creation and use of human embryos by fertilisation of a human egg by a human IVD sperm, fertilisation of a human IVD egg by human sperm, and fertilisation of a human IVD egg with human IVD sperm, in each case provided that the sperm and egg are not derived from the same person.

Recommendation 12: The legislation should be amended to include a definition of IVD gametes. Such a definition could be 'human sperm or eggs derived from precursor cells or by *in vitro* means'.

Recommendation 13: Section 20(4) of the *Prohibition of Human Cloning for Reproduction Act 2002* should be amended to include embryos created with the use of IVD sperm or eggs in the definition of 'prohibited embryo'. Such a definition could include 'hybrid embryos within the meaning of s 8 of this Act'.

Recommendation 14: The *Prohibition of Human Cloning for Reproduction Act 2002* should be amended to extend the definition of 'hybrid embryos' to include an embryo created by the use of IVD gametes. Such a definition could be 'In the foregoing human egg or human sperm includes IVD gametes'.

Recommendation 15: Section 21 of the *Prohibition of Human Cloning for Reproduction Act 2002* should be amended to include IVD gametes.

Recommendation 16: There should be no specific definition of human sperm and egg.

Recommendation 17: The *Prohibition of Human Cloning for Reproduction Act 2002* should be amended to include a definition of fertilisation.

Recommendation 18: Section 8 of the *Research Involving Human Embryos Act 2002* should be amended to clarify who is required to give consent in relation to donation of fetal tissues and who is required to give consent in relation to donation of failed-to-fertilise or abnormally fertilised eggs.

Recommendation 19: Section 24(5) of the *Research Involving Human Embryos Act 2002* should be amended to provide that a condition of a licence may include a limitation on the number of embryos or eggs for which consent is to be obtained prior to research use.

Recommendation 20: When the current NHMRC *Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research* undergo review, consideration should be given to including guidance that excess embryos donated for research should be kept in storage for a maximum of five years, after which their custodians should arrange for the respectful disposal of these embryos. Consideration should also be given to guidance that respectful disposal of these embryos should occur if it becomes clear even within that five year period that these embryos are most unlikely to be used in research.

Recommendation 21: The term 'significant advance' in s 21(4) of the *Research Involving Human Embryos Act 2002* should not be the subject of legislative definition.

Recommendation 22: Section 21(2) of the *Research Involving Human Embryos Act 2002* should be amended to provide that the Licensing Committee may require that an application be withdrawn if the Licensing Committee does not have sufficient information to allow it to make a decision to issue or not issue a licence.

Recommendation 23: Section 26 of the *Research Involving Human Embryos Act 2002* should be amended to provide that the Licensing Committee may, by notice in writing to the licence holder, suspend or revoke a licence if it considers that the endpoints of the licensed activity have been achieved or that the licensed activity no longer would be expected to lead to a significant advance.

Recommendation 24: Section 26 of the *Research Involving Human Embryos Act 2002* should be amended to provide that the Licensing Committee may, by notice in writing to the licence holder, suspend or revoke a licence if the Licensing Committee believes on reasonable grounds it is necessary or desirable to do so.

Recommendation 25: Section 27 of the *Research Involving Human Embryos Act 2002* should be amended to provide that a licence may only be surrendered with the prior consent of the Licensing Committee.

Recommendation 26: Section 21(3)(c) of the *Research Involving Human Embryos Act 2002* should be amended to provide that a HREC should have regard, amongst other things, to the matters which the Licensing Committee itself must have regard under s 21(3) and s 21 (4).

Recommendation 27: There should be no change to the categories of membership of the Licensing Committee.

Recommendation 28: Note (b) to s 23B(3) of the *Prohibition of Human Cloning for Reproduction Act 2002* should be amended to reflect s 20(1)(f) of the *Research Involving Human Embryos Act 2002.*

Recommendation 29: Sections 26(2) and 41 of *Research Involving Human Embryos Act 2002* should be amended to refer to the *Prohibition of Human Cloning for Reproduction Act 2002*.

Recommendation 30: The *Research Involving Human Embryos Act 2002* and the *Prohibition of Human Cloning for Reproduction Act 2002* should be amended to make reference to the *Ethical guidelines on the use of assisted reproductive technology in clinical practice and research* and the *National statement on ethical conduct in human research* as in force from time to time.

Recommendation 31: The *Research Involving Human Embryos Act 2002* and the *Prohibition of Human Cloning for Reproduction Act 2002* should be amended to make reference to a National Stem Cell Bank instead of a National Stem Cell Centre.

Recommendation 32: Schedule 1 of the *Research Involving Human Embryos Act 2002* should be updated to list the following prescribed bodies:

- The Australian Academy of Science
- ACCESS Australia's National Infertility Network Ltd
- CHOICE
- The Australian Research Council
- Universities Australia
- Consumers Health Forum of Australia
- The Law Council of Australia
- The Australian Federation of Disability Organisations
- The Royal College of Nursing, Australia
- The Australasian Association of Bioethics and Health Law
- The Australian Society for Medical Research
- The Fertility Society of Australia
- The Royal Australasian College of Physicians
- The Royal Australian and New Zealand College of Obstetricians and Gynaecologists
- The Royal Australian College of General Practitioners
- The Society for Reproductive Biology

Recommendation 33: The *Research Involving Human Embryos Act 2002* and the *Prohibition of Human Cloning for Reproduction Act 2002* should be amended to provide for a review of these Acts be undertaken at five year intervals.

4. STATUTORY CRITERIA

4.1 Developments in Assisted Reproductive Technology (ART)

Since the first successful pregnancy from *in vitro* fertilisation (IVF) in 1978, there have been significant advances in ART techniques that have led to IVF becoming a routine procedure available for people with fertility problems.

4.1.1 Current Methods of Overcoming Fertility Problems ART

Several methods are currently used throughout Australia to assist couples in overcoming fertility problems. ART predominantly covers induction of ovulation, sperm preparation, artificial insemination and IVF.

The primary procedures used in ART include artificial insemination, IVF, intracytoplasmic sperm injection (ICSI), gamete intrafallopian transfer (GIFT), embryo freezing and replacement, blastocyst culture, assisting hatching and genetic testing.

IVF is still the predominant form of ART treatment. This treatment requires a significant time involvement; however, success rates have increased over time.

ICSI is usually conducted if fertilisation through IVF has not resulted in a pregnancy. It is predominantly used for males with a low sperm count. This form of ART requires minimal sperm and egg donation from the couple to form an embryo. Essentially a single viable sperm is injected into a single mature egg.[1]

Embryo freezing and replacement transfer is the storing of embryos for possible future implantation. Under the current legislation, embryos can be stored for up to ten years in Australia. These can be thawed and replaced in normal cycles, greatly simplifying the patient's treatment cycle and costs. Success rates for pregnancy from frozen embryos are generally not as high as for IVF, however, advances in technology have decreased the margin of difference between the two techniques.[2]

4.1.2 Improved Culture Media and other ART Procedures

Improving culture media for developing ART embryos is an important focus of research and of, ART therapies because suboptimal culture conditions result in an increased rate of fetal abnormalities, and a lower rate of implantation and fetal survival.

[1] Elder K et al. (2011). *In-Vitro Fertilization*. Cambridge University Press.

[2] ibid.

Research is ongoing to improve methods of collection, preservation and *in vitro* maturation of gametes. *In vitro* maturation of eggs, which would avoid the problem of drug-induced egg maturation *in vivo*, has been used successfully in mice.

Since 2005, there have been major advances in freezing eggs. Since 2007, about 200 babies have been born from cryo-preserved eggs.[3] Improved methods for freezing ovarian and testicular tissues are also being investigated.

4.1.3 Embryo Selection

Selection of high-quality embryos is an important aspect of ART treatment. Since 2005, there have been further improvements in implantation and pregnancy rates using single-embryo transfer.[4]

4.1.4 Pre-Implantation Genetic Testing

Since 2005, the use of pre-implantation genetic testing has increased to select healthy embryos for transfer. Development of improved molecular diagnostic tools has reduced the likelihood of PGD misdiagnosis.[5] Pre-implantation genetic diagnostic (PGD) tests are used to detect specific genetic mutations. Pre-implantation genetic screening (PGS) is used to screen for chromosome aneuploidies.

Recently, blastocyst stage biopsy (removal of cells from a blastocyst at 5–6 days of development) is replacing blastomere biopsy (removal of cells at about 3 days post fertilisation) to obtain cells for genetic testing. This technique is thought to be safer because the inner cell mass is not disturbed. Also, since more than one cell is taken, the sensitivity of PGD is increased.[6]

4.1.5 *In vitro* Derived (IVD) Gametes

Recent research into IVD gametes has shown that gametes (sperm and eggs) can be derived from other types of cells. These cells include stem cells, precursor cells from fetal tissue, and cells produced by experimentally halving the number of chromosomes in somatic cells (somatic cell haploidization). In consequence, embryos could in the future, at least in theory, be derived from a person's body cells rather than from their sperm or egg.

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[3] Bagchi A. (2008). *Cryopreservation and vitrification: recent advances in fertility preservation technologies*. Expert Review of Medical Devices 5(3): 359-70

[4] Elder K et al. (2011). *In-Vitro Fertilization*. Cambridge University Press.

[5] Yosef B et al. (2008). PGD-derived human embryonic stem cell lines as a powerful tool for the study of human genetic disorders. Molecular and Cellular Endocrinology 282(1-2):153–158.

[6] McArthur S. (2008). Blastocyst trophectoderm biopsy and preimplantation genetic diagnosis for familial monogenic disorders and chromosomal translocations. Prenatal Diagnosis 25(5): 434-442.

Animal ES cells have been differentiated *in vitro* to form gametes. Mouse ES cells can develop into primordial germ cells, gametes and blastocysts. In 2006, in one mouse study, ES cell-derived sperm cells fertilised eggs and supported development of mouse pups to term.[7]

IVD gamete research provides an avenue of research to assist infertile couples to have their own biological children. Several methods are being researched, to date only in animals, including differentiating stem cells to form gametes. However, there are major technical, safety, legal and ethical issues to overcome before these methods can be used clinically if that should ever become possible.

4.2 Developments in ES Cell Research

Presently, there are three types of human stem cell being examined for their potential medical research value: adult stem cells, taken from the body, such as bone marrow or umbilical cord blood; ES cells extracted from human embryos, including embryos formed by SCNT; and iPS cells which are adult cells that have been genetically altered to resemble ES cells.

4.2.1 Adult Stem Cells

The term 'adult stem cell' is probably inappropriate as cells of this type are found also in fetuses and children. They are more differentiated than ES cells, and can generate a more restricted range of tissue types.

Transplantation of cell populations which include adult stem cells has been routinely used clinically for many years. Examples include bone marrow replacement after chemotherapy and in the course of skin grafting for burns treatment.

Additionally, use of cell populations derived from isolated adult stem cells for the treatment of other diseases is the subject of extensive clinical research. A possible future use of human adult stem cells would be to repair the tissue or organ they are derived from. Ideally, the stem cells would come from the patient or a genetically identical twin, though cells from closely genetically related individuals can be used in conjunction with immunosuppression.

[7] Chunli Zhao Y. (2007). *Establishment of customized mouse stem cell lines by sequential nuclear transfer.* Cell Research 17: 80–87.

One research use of adult stem cells has been to understand the role of stem cell function in health and disease states. Adult stem cell research has significantly advanced areas of cancer research[8] and tissue generation and repair.[9]

Scientists from Cambridge[10] and Edinburgh Universities[11] have discovered a way of stimulating rat brain adult stem cells with retinoic acid to help repair damaged myelin. Such research could eventually lead to the development of drugs that repair nerves in the brain and spinal cord and potentially reverse some of the symptoms of multiple sclerosis.

Two groundbreaking studies show that doctors have used adult stem cells from bone marrow to help heal children with a rare skin disease[12] and repair injured lungs.[13] One study shows the treatment for skin disease has worked to varying degrees for most of the children.[14] While not a cure, the technique has improved patients' mobility and ability to eat. In another study, University of California researchers found bone marrow stem cells can restore damaged lungs. They hope to prove the therapy is viable for preventing respiratory failure in critically ill patients.[15]

In an adult stem cell-based clinical trial in the United Kingdom, scientists announced they had placed approximately 2 million laboratory-cultured adult

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[8] Lim E et al. (2009). *Aberrant luminal progenitors as the candidate target population for basal tumor development in BRCA1 mutation carriers.* Nature Medicine 15: 907-913.

[9] *Australian Life Scientist. (2011). Mesoblast sees positive interim results from heart stem cell trial.* Retrieved from: http://www.lifescientist.com.au/article/372982/mesoblast_sees_positive_interim_results_from_heart_stem_cell_trial/; Genetic Engineering & Biotechnology News. (2010). *Prochymal new drug submission granted priority review by Health Canada.* Retrieved from: http://www.genengnews.com/industry-updates/prochymal-new-drug-submission-granted-priority-review-by-health-b-b/89258506/; Di Girolamo N et al. (2009). *A contact lens-based technique for expansion and transplantation of autologous epithelial progenitors for ocular surface reconstruction.* Transplantation 87(10): 1571-1578; Dayton L. (2009). *Stem cells used to restore sight for corneal disease suffers.* The Australian. Retrieved from: http://www.theaustralian.com.au/news/nation/stem-cells-used-to-restore-sight-for-corneal-disease-sufferers/story-e6frg6nf-1225717205094.

[10] Mi S. (2007). *LINGO-1 antagonist promotes spinal cord remyelination and axonal integrity in MOG-induced experimental autoimmune encephalomyelitis.* Nature Medicine 13: 1228-1233.

[11] Huang JK. (2011). *Retinoid X receptor gamma signaling accelerates CNS remyelination.* Nature Neuroscience 14: 45–53.

[12] Xiaohui F et al. (2010). *Allogeneic human mesenchymal stem cells restore epithelial protein permeability in cultured human alveolar type II cells by secretion of angiopoietin-1.* Journal of Biological Chemistry 285: 26211-26222.

[13] Wagner J et al. (2010). *Bone Marrow Transplantation for Recessive Dystrophic Epidermolysis Bullosa.* New England Journal of Medicine 363(7): 629–639.

[14] Ibid.

[15] Xiaohui F et al. (2010). *Allogeneic human mesenchymal stem cells restore epithelial protein permeability in cultured human alveolar type II cells by secretion of angiopoietin-1.* Journal of Biological Chemistry 285: 26211-26222.

stem cells derived from the brain directly into damaged brain tissue in an elderly man.[16] This University of Glasgow trial intends to establish the safety of the surgical procedure. Developed by British company ReNeuron, the source of the stem cells and the manner of their preparation has meant that trial patients do not require anti-rejection drugs, which can increase the risk of a cancer arising from the adult stem cell.[17]

According to research at the University of Pittsburgh Schools of the Health Sciences, experiments conducted indicate that adult stem cells collected from human corneas could restore transparency and would not trigger a rejection response when injected into eyes that are scarred and hazy.[18]

In Australia, Sydney researchers have been able to achieve a threefold increase in human bone marrow derived adult stem cells, an advance that may be useful in the treatment of many blood disorders.[19]

In addition, a very promising area of adult stem cell research is in the area of mesenchymal stem cells (MSC), which are intermediate between pluripotent ES cells and single organ derived stem cells in their capacity to form different tissues or organs. Mesenchymal stem cells have the advantage that, unlike iPS and ES cells, they are unlikely to form tumours on implantation. Additionally, they appear to be less subject to rejection by the immune system of an unrelated recipient. Much work is occurring overseas and within Australia in this area.[20]

4.2.2 iPS Cells

The first report of the 'reprogramming' of mouse skin cells into stem cells was in 2006 by a team led by Shinya Yamanaka at Kyoto University.[21] A year later, Yamanaka's team and another team led by James Thomson at the University of Wisconsin, reported success with human cells.[22]

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[16] Sample I. (2011). *Neural stem cells injected into the brain of a stroke patient in world first.* Guardian News and Media Limited. Retrieved from: http://www.guardian.co.uk/science/2010/nov/16/stem-cells-injected-brain-stroke.

[17] Ibid.

[18] University of Pittsburgh Schools of the Health Sciences. (2009). *Stem Cell Therapy Makes Cloudy Corneas Clear.* ScienceDaily. Retrieved from: http://www.sciencedaily.com/releases/2009/04/090409103350.htm.

[19] Holst J. (2010). *Substrate elasticity provides mechanical signals for the expansion of haemopoietic stem and progenitor cells.* Nature Biotechnology 28(10):1123-1128.

[20] Chamberlain G. (2007). *Concise Review: Mesenchymal Stem Cells: Their Phenotype, Differentiation Capacity, Immunological Features, and Potential for Homing.* Stem Cells 25(11): 2739-2749.

[21] Takahashi K. (2006). *Induction of Pluripotent Stem Cells from Mouse Embryonic and Adult Fibroblast Cultures by Defined Factors.* Cell 126(4): 663-76.

[22] Yu J. (2007). *Induced Pluripotent Stem Cell Lines Derived from Human Somatic Cells.* Science 318(5858): 1917-1920.

All ES cell populations, however derived, have the potential to differentiate to cancer *in vivo.* The initial technique used to produce iPS cells required a gene product that could also enhance the risk of the iPS cells transforming to cancer cells.

From 2008 onwards, several articles have been published identifying other possible ways of developing iPS cells with less potential for promoting cancer development. These included activating a protein after the transformation of the cells was complete. However, as for other pluripotent stem cells, the risk of a cancer arising from the cells once placed in the body will remain, if the cells are not completely differentiated *in vitro* before their therapeutic use.

The iPS cells hold great promise for research and for regenerative medicine, as in principle cells, tissues or organs derived from these cells should not be rejected by the immune system of the person from whom they are derived. However, recent research suggests that iPS cells generated by currently available technologies are susceptible to immune-mediated rejection under some circumstances.[23]

In October 2010, Australian researchers developed the country's first diabetes-specific stem cell line through iPS cell technology.[24]

Recently scientists from Monash University and CSIRO have reported generating iPS cells from human kidney cells.[25]

iPS cell technology has also been used to generate several disease-specific cell lines for diseases such as Parkinson's Disease[26], spinal muscular atrophy[27], Huntington's Disease[28] and Down's Syndrome.[29]

Research on iPS cells may eventually lead to the development of patient-specific stem cell lines which could be used clinically without the need to

[23] Hayden E. (2011). *Reprogrammed cells trigger immune reactions in mice.* Nature News. Retrieved from: http://www.nature.com/news/2011/110513/full/news.2011.286.html.

[24] State Government Victoria. (2010). *Australian stem cell line offers fresh approach to diabetes cure.* Invest Victoria Australia. Retrieved from: http://www.invest.vic.gov.au/20101022-australian-stem-cell-line-offers-fresh-approach-to-diabetes-cure.

[25] Song B et al. (2011). *Generation of Induced Pluripotent Stem Cells from Human Kidney Mesangial Cells.* Journal of the American Society of Nephrology. Published online before print May 12, 2011, doi: 10.1681/ASN.2010101022. Retrieved from: http://jasn.asnjournals.org/content/early/2011/05/12/ASN.2010101022.abstract

[26] Soldner F et al. (2009). *Parkinson's Disease Patient-Derived Induced Pluripotent Stem Cells Free of Viral Reprogramming Factors.* Cell 136(5): 964–977.

[27] Ebert A et al. (2009). *Induced pluripotent stem cells from a spinal muscular atrophy patient.* Nature 457: 277-280

[28] Park I.H at el. (2008). *Disease-Specific Induced Pluripotent Stem Cells.* Cell 134(5): 877-886

[29] Ibid.

use human eggs or embryos. However, additional research is required to establish whether iPS cells are sufficiently similar to ART derived ES cells to be functional equivalents.

4.2.3 SCNT Derived ES Cells

The *Research involving Human Embryos Act 2002*, regulating the use of human embryos for research, was amended in 2006 to enable research using human embryos created using SCNT. SCNT comprises the transfer of the nucleus of a human adult somatic cell (a cell other than a sperm or egg) into a human egg whose nucleus has been removed.

This legislative amendment was made in light of the possibility of using this technique to provide patient matched cells for use in research and treatment of human disease, and in the absence of any other obvious method to produce pluripotent human stem cells from tissue that would be matched to a potential recipient of cell, tissue or organ replacement therapy. The amendment was justified by the successful use of this technique in animals to generate:

- viable blastocysts which when reimplanted into an appropriate host uterus gave rise, with low efficiency, to viable progeny.
- ES cell lines which passed three tests of validity – capacity to produce all embryonic layers, capacity to grow as teratomas (undifferentiated tumours) in immunosuppressed hosts, and capacity when injected into blastocysts to create chimeric animals in which the ES cells could be demonstrated to contribute to all host tissues including germ cells, and hence eventually to whole animals.
- a small number of animal experiments in which tissue had been regenerated using transfer of ES cells derived by SCNT, although rejection has occurred in some cases.

Attempts to generate human ES cells by SCNT have been pursued for over seven years and, with the notable exception of work reported from Korea and subsequently admitted to be fraudulent,[30] are yet to produce a claim to development of a human ES cell line, though development of embryos to the eight cell stage has been achieved.[31]

Since 2006, SCNT has continued to be used for animal cloning work, including livestock cloning, wildlife cloning and cloning laboratory animals for research. Research has continued to focus on methods to increase the rate of blastocyst formation, implantation and healthy offspring. However, cloning efficiency

[30] Kennedy D. (2006). *Editorial Retraction.* Science. 311(5759): 335.

[31] Antonia A et al. (2009). *Stem Cell and Regenerative Medicine.* Current Stem Cell Research & Therapy 4: 287-297.

continues to be low: about 2 per cent for reproductive cloning in animals and up to 20 per cent for blastocyst development for ES cell research.[32]

Difficulties with human SCNT have been the catalyst for much other research on cellular, molecular and genetic processes.[33] This research has increased the understanding of epigenetics (the changes in the state of a gene's expression without changes to the DNA sequence itself) and of interactions between mitochondrial DNA and nuclear DNA. [34]

Modifications to SCNT methodology have allowed the successful creation of non-human primate SCNT embryo clones and SCNT derived ES cell lines. However, the efficiency was low; more than 300 eggs were used to derive two SCNT derived ES cell lines.[35]

In 2008, researchers reported successfully using SCNT to produce human blastocyst stage embryos, but have not yet established any SCNT derived ES cell lines.[36]

Since 2005, many studies have demonstrated the feasibility of animal–animal interspecies SCNT (e.g. cow eggs and nuclei from other species) for early embryo development but not for reproductive cloning apart from some cases of very closely related species. [37]

More recently, some researchers have reported successful development of animal–human interspecies SCNT (iSCNT) embryos using human nuclei and cow eggs. Animal–human iSCNT provides an opportunity to study interactions between the nucleus and the cytoplasm, and to investigate early human embryo development without the need for human eggs. However, early studies have shown that using animal eggs brings its own set of molecular and genetic issues that need further research. [38]

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[32] Campbell K et al. (2007). *Somatic cell nuclear transfer: Past, present and future perspectives.* Theriogenology 68(1): 214-231.

[33] Henderson J. (2008). *Lazarus's Gate: Challenges and Potential of Epigenetic Reprogramming of Somatic Cells.* Clinical Pharmacology & Therapeutics 83(6): 889–893.

[34] Hiendleder S at el. (2007). *Mitochondrial DNA Inheritance after SCNT.* Advances in Experimental Medicine and Biology 591:103-116.

[35] Byrne J at el. (2007). *Producing primate embryonic stem cells by somatic cell nuclear transfer.* Nature 450:497–502.

[36] French A at el. (2008). *Development of Human Cloned Blastocysts Following Somatic Cell Nuclear Transfer with Adult Fibroblasts.* Stem Cells 26(2): 485-493.

[37] Fuchs E. (2008). Stem Cells: Biology, Ethics and potential for Medicine. Collège de France. Retrieved from : http://annuaire-cdf.revues.org/266.

[38] Chung Y at el. (2009). *Reprogramming of Human Somatic Cells Using Human and Animal Oocytes.* Cloning and Stem Cells 11(2): 213-223.

Current evidence suggests that the process of generating animal ES cells by SCNT shares, with the process of generating iPS cells, the possibility of causing genetic and epigenetic modifications to DNA that restrict the capacity of these cells to have the full potential of ES cells generated from ART embryos.

4.2.4 Applications of ES Research

Embryonic stem cell research has been extremely active since 2005, with most international effort focusing on the development of culture conditions for maintaining well-characterised ES cells and for differentiating them into cell types with potential for research and safe clinical use.

Australian research is contributing to the international effort in this area with the production, under licence, of several well characterised cell lines. Several ES cell lines have been sent to collaborators locally and worldwide for use in basic research, disease modelling and therapeutic research.

Australian research is also contributing to the derivation of human ES cells from embryos identified through PGD to be affected by known genetic conditions. Under certain licenses granted in Australia through the Licensing Committee, 15 disease specific ES cell lines have been derived and six new putative disease specific ES cell lines have been derived. These cell lines are currently undergoing characterisation to define their properties.[39] These ES lines are useful for research on the genetic condition and for development of new drugs and diagnostic tools for the condition.

The clinical application of ES cells, however derived, is the generation of cells, tissues or organs for repair purposes. To avoid the risk of rejection, the ES cell line is ideally derived from the potential tissue recipient using SCNT derived ES cells or iPS cells. To avoid the risk of tumour development, the cells need to be differentiated *in vitro*, and this process needs to be achieved reliably and demonstrably for all cells in the culture. The following are some examples of what has recently been achieved.

Researchers at the University of California have created early-stage retinas from human ES cells and these are now being tested in animal models. This is fundamental research that marks the first steps in development to transplant-ready retinas to treat eye disorders.[40]

Researchers at Harvard University have created a strip of pulsating heart muscle from mouse ES cells.[41] This has resulted in several other developments

[39] National Health and Medical Research Council. (2010). *NHMRC Embryo Research Licensing Committee report to the Parliament of Australia for the period 1 March 2010 to 31 August 2010.*

[40] UCI Irvine Today. (2010). *UCI researchers create retina from human embryonic stem cells.* Retrieved from:<http://today.uci.edu/news/2010/05/nr_retina_100526.php>.

[41] Domain I et al. (2009). *Generation of Functional Ventricular Heart Muscle from Mouse Ventricular Progenitor Cells.* Science 326(5951): 426-429..

using mice models, such as using vascular cells derived from umbilical cord stem cells to develop tissue patches for the damaged hearts of mice. This is a vital step towards growing replacement parts for hearts damaged by disease.[42]

At the Salk Institute (in the US), researchers have been able to develop ES cells into the cells that are involved in the motor neurone disease, amyotrophic lateral sclerosis (ALS).[43] ALS is a debilitating degenerative disease that currently has no cure or treatment. These ALS cell lines will be used to screen drugs that may be able to treat ALS.

Considerable progress has been made in creating pancreatic cells from human ES cells. [44] Though insulin-producing cells have been developed, they do not yet respond appropriately to extracellular glucose, a prerequisite for their use to treat patients with type 1 (juvenile) onset diabetes.[45]

In Australia, researchers have derived four human ES cell lines from embryos identified as affected by Huntington's disease. These lines will be used to further examine the disease and to develop potential treatments.[46]

The first clinical trial resulting from human ES cell research commenced in October 2010. This trial, conducted by Geron, resulted from research at the Shepherd Center in the United States.[47] The primary objective of this study is to assess the safety and tolerability of GRNOPC1, a human ES cell-derived cell aimed at treating patients with acute spinal cord injury. A larger trial is planned to assess whether the treatment will restore function. It will be several years before the outcomes of this further trial are fully known. However, reports have indicated that the results thus far have been promising and no adverse side effects have been noted.

In November 2010 and January 2011 two additional early-phase clinical trials conducted by Advanced Cell Technology Inc in the United States have been

[42] University of Washington. (2009). *Major Improvements Made in Engineering Heart Repair Patches From Stem Cells.* ScienceDaily. Retrieved from: <http://www.sciencedaily.com/releases/2009/10/091007124721.htm>

[43] Hedlund E et al. (2008). *ALS model glia can mediate toxicity to motor neurons derived from human embryonic stem cells.* Cell Stem Cell 3(6):575-576.

[44] Kroon E et al. (2008). *Pancreatic endoderm derived from human embryonic stem cells generates glucose-responsive insulin-secreting cells in vivo.* Nature Biotechnology 26: 443-452.

[45] Skyler J et al. (2011). *Stopping Type 1 Diabetes: Attempts to Prevent or Cure Type 1 Diabetes in Man.* American Diabetes Association 60(1): 1-8.

[46] Bradley CK et al. (2011). *Derivation of Huntington's Disease-affected human embryonic stem cell lines.* Stem Cells and Development 20(3): 495-502.

[47] Geron Corporation. (2010). ABOUT GRNOPC. Retrieved from: http://www.geron.com/GRNOPC1Trial/grnopc1-intro.html.

approved.[48] These trials will use human ES cells to treat age-related blindness in adults (age-related macular degeneration) and a rare form of juvenile blindness termed Stargardt's disease that affects children as young as six years old. Again, the initial aim of these early phase trials is to test the safety of the therapy, which uses human ES cells differentiated *in vitro* to recreate retinal pigment epithelial cells.[49]

4.2.5 Mitochondrial Disorders

Mitochondria are small structures found in the cytoplasm of human cells that enable the process in which molecules from food are converted into high-energy molecules. They are essential for functions such as cell reproduction, transportation of materials, and protein synthesis.

Inherited mitochondrial disorders are rare, debilitating and sometimes lethal. There is currently no cure. One set is due to faulty genetic information in mitochondrial DNA, which is inherited by a child solely from its mother, although not all offspring of a mother with a genetic disorder of her mitochondrial DNA will be equally affected.

The symptoms of mitochondrial disorders are diverse, progressive and include loss of motor control, liver disease, visual or hearing loss and intellectual impairment. Between 200 and 300 Australian families are affected by these disorders.[50]

In theory, an affected mother could have a child that had her and her partner's genes, but without the mitochondrial disorder, by creating an embryo where the mitochondria came from an egg from an unaffected donor. The nucleus from an egg, fertilised *in vitro* by her partner's sperm, would be transferred to the unaffected enucleated egg using a variation of SCNT. The complex nature of mitochondrial biology complicates this process, as partial mitochondrial replacement is possible, which may not prevent occurrence of the disease in the child.

4.3 Community Standards

In 2004, a study by Swinburne University of Technology found that 63 per cent of respondents were opposed to ES cell research. In 2005, a study by

[48] Advanced Cell Technology. (2010). *ACT Files European Clinical Trial Application for Phase 1/2 Study Using Embryonic Stem Cells to Treat Macular Degeneration*. Retrieved from: http://www.advancedcell.com/news-and-media/press-releases/act-files-european-clinical-trial-application-for-phase-12-study-using-embryonic-stem-cells-to-treat-/.

[49] ibid

[50] Katsnelson A. (2010). *Freeing human eggs of mutant mitochondria*. Nature News. Retrieved from: http://www.nature.com/news/2010/100414/full/news.2010.180.html.

Southern Cross Bioethics Institute found that 55 per cent were opposed to ES cell research.[51]

In 2005, 2007 and 2010, the Commonwealth Department of Innovation, Industry, Science and Research conducted studies into public attitudes towards applications of biotechnology.[52]

These studies consisted of three phases aimed at engaging the most accurate information regarding public attitudes towards biotechnology applications. The first phase included group discussions with a variety of demographics including engaging respondents with tertiary and non- tertiary backgrounds and also from various age brackets. Stakeholder consultations were also undertaken with Government, industry and non-government organisations. The final phase was a survey consisting of a national random sample of over 1,000 people.

The Review Committee believes that awareness of ES research is high, and has not recently changed significantly. Responses to these studies can be summarised as follows:

- awareness of using stem cells to conduct medical research or treat diseases was 90 per cent in 2007 and 93 per cent in 2010;
- awareness of conducting medical research on treating diseases using ES cells was 84 per cent in 2007 and 80 per cent in 2010;
- awareness of using non-embryonic, cord or adult cells was 67 per cent in 2007 and 66 per cent in 2010;
- appreciation of a benefit in using stem cells to conduct medical research and treat disease was 90 per cent in 2007 and 91 per cent in 2010;
- respondents identifying ES cell research as not useful was 12 per cent in 2007 and 9 per cent in 2010;
- no significant changes were reported in regards to acceptability of overall stem cell applications; and
- in 2010, survey respondents were asked if they understood the term 'cloning of human embryos'. Of the respondents, 30 per cent said they knew enough about the term to explain it to a friend, 57 per cent had heard of it but knew very little or nothing about it, 12 per cent had heard of it and only 1 per cent said they did not know the term.

[51] Swinburne University of Technology. (2004). *Understanding Australians' Perceptions Of Controversial Scientific Research.* Australian Journal of Emerging Technologies and Society 2(2): 82-107.

[52] Further information and reports relating to the 2005, 2007 and 2010 Department of Innovation, Industry, Science and Research community attitudes towards biotechnology research projects can be found at:. *Research and Reports.* Department of Innovation, Industry, Science and Research from: http://www.innovation.gov.au/Industry/Nanotechnology/PublicAwarenessandEngagement/Pages/ResearchandReports.aspx

In 2010, respondents were also asked what they perceive to be the impact of cloning of human embryos on our way of life. Only 28 per cent said it would improve our way of life, 9 per cent said it would have no effect, 46 per cent said it would make things worse, and 17 per cent did not know. The closest comparable question from 2005 related to the perceived impact of cloning, to which 19 per cent said it would improve our way of life, 10 per cent said it would have no effect, 58 per cent said it would make things worse and 13 per cent were uncertain.

Support for using stem cells to conduct medical research and treat diseases has increased since 2005, as has support for using non-embryonic or adult stem cells.[53] In 2010, 17 per cent of the population did not accept using them, contrasting with 24 per cent of the population in 2005.

4.4 International Developments

In general, many countries have adopted legislative controls that ban some practices and licence others under the supervision of specialist bodies.

4.4.1 Legislative Structures

In addition to Australia, countries that allow the derivation of human ES cells from excess ART embryos and embryos created via SCNT, and are therefore considered to employ permissive regulation include United Kingdom, Spain, Israel, Sweden, China, India, South Korea, USA and Singapore.

Countries that allow the derivation of human ES cells but not SCNT include Canada, France and Brazil.

Countries that employ restrictive policies include Germany and Italy. German researchers are only permitted to conduct research on imported and existing human ES cell lines created before 2007. Italian researchers are only permitted research on imported human ES cell lines.

4.4.2 United Kingdom

In the United Kingdom (UK), the legislative and regulatory framework governing ES cell research is complex due to the numerous governmental bodies involved in the licensing and research approval process. The *Interim UK Regulatory Route Map for Stem Cell Research and Manufacture* identifies that the appropriate regulatory route depends on whether the stem cells are intended for human application, derived from human embryos, are genetically modified or intended to be manufactured into a medical product.

[53] Swinburne University of Technology. (2004). *Understanding Australians' Perceptions Of Controversial Scientific Research.* Australian Journal of Emerging Technologies and Society 2(2): 82-107.

The derivation of human ES cells is controlled and regulated by the *Human Fertilisation and Embryology Act 1990*, as amended by the *Human Fertilisation and Embryology Act 2008*. Under these acts, the Human Fertilisation and Embryology Authority (HFEA) is responsible for the licensing of human embryo research and the regulation of embryo and gamete storage.

Despite the strict regulation of ES cells, the derivation of iPS cells is not regulated under the Act. As in Australia, the absence of legislative cover is a consequence of iPS cells not being derived from embryos.

However, in contrast to Australia, the UK *Human Fertilisation and Embryology Act 2008* regulates the use of IVD gametes for reproductive purposes. In the UK, no restrictions are placed on the *in vitro* derivation of artificial gametes, but the use of such gametes in reproduction is prohibited. Artificial gametes may only be used under licence to create an embryo up to the limit of 14 days *in vitro*.

At the time of the Lockhart Review and after changes to the Australian legislation, the UK legislation did not expressly prohibit the use of animal eggs in SCNT. In November 2006, two UK research teams applied for licences to the HFEA seeking to use animal eggs in SCNT. A Parliamentary debate and HFEA public consultation followed.

HFEA permitted research applications to be made for the creation of animal-human embryos, where the intended research is 'necessary and desirable'. Subsequently, the UK Parliament amended the legislation to allow animal-human embryo research under a licence.

Under the UK licensing scheme permission may be granted for SCNT, the creation of fresh embryos and cybrids. Research into treatment for mitochondrial disease is currently under review.

In January 2011, HFEA launched a public consultation process in relation to consent for sperm and egg donation for IVF including the level of compensation for donors, the number of families a donor can help to create and family donation. The results of this process are due to be released later this year.

4.4.3 Canada

The Canadian regulation of ES cell research is more restrictive than Australia's in that it does not allow the creation of embryos by SCNT. Modelled on the UK legislation, the Canadian *Assisted Human Reproduction Act 2004* establishes a national regulatory scheme for the regulation of reproductive technologies, cloning and related stem cell research. Although research on spare IVF embryos is permitted, criminal sanctions apply to the creation of embryos by SCNT.

Research on human stem cells must be undertaken in accordance with national research ethical guidelines ie. the Tri-Council Statement: *Ethical Conduct for Research Involving Humans* (TCPS) and the Canadian Institutes of Health Research (CIHR) updated *Guidelines for Human Pluripotent Stem Cell Research.*

In contrast to Australia, the CIHR Guidelines apply specifically to any CIHR-funded research involving human pluripotent stem cells, regardless of their source and thus cover the regulation of iPS cells.

4.4.4 United States

Except for the restrictions on the use of federal funds for human embryonic research, the United States does not have Federal legislation governing human embryo research, including human cloning for research. Some individual states including California, New York, and Connecticut have introduced permissive legislation while some other States have restrictive legislation.

Restrictions were imposed by the Bush Administration on the use of excess human embryos from IVF in research, restricting research to a specific number of stem cell lines derived before 2001.

In 2009, President Barack Obama lifted this Federal restriction. However, the use of Federal funding has been restricted due to the law known as the Dickey-Wicker Amendment[54] which forbids the use of Federal funds for research that destroys an embryo. The National Institutes of Health (NIH) may fund research involving approved ES cell lines but not the creation of new ES cell lines.

A Federal judge granted a preliminary injunction restraining the NIH from funding research using human ES cells. On 29 April 2011 this injunction was set aside by the Court of Appeals for the District of Columbia Circuit. A majority of the court held that the plaintiffs were unlikely to prevail at trial because the Dickey-Wicker Amendment was ambiguous and the NIH had reasonably concluded that, although the Dickey-Wicker Amendment barred funding for the destructive act of deriving ES cells from an embryo, it does not prohibit funding research in which an ES cell will be used.[55]

[54] Genetics and Public Policy Centre. (2010). *Cloning Dickey-Wicker Amendment [United States].* Retrieved from http://www.dnapolicy.org/policy.international.php?laws_id=36&action=detail.

[55] United States Court of Appeals. (2011). *Sherley v Secretary of Department of Health and Human Services.* No 10-5287.

4.4.5 International Legislation Relating to the Provision of Valuable Consideration for Egg Donation

Australian legislation, through s 21 of the *Prohibition of Human Cloning for Reproduction Act 2002*, prescribes the prohibition of the provision of valuable consideration for egg donation, which indicates compensation can be provided for reasonable expenses only.

The *Human Fertilisation and Embryology Act 2008* in the UK also permits the reimbursement of payment for reasonable expenses only. However, the UK also permits 'egg sharing', where women are offered financial incentive of cheaper IVF treatment in return for 'donating' a proportion of their eggs for research.

In the United States, the National Academy of Sciences *Guidelines for Human Embryonic Stem Cell Research* recommends that women should not be paid beyond direct expenses to donate eggs for research. However, this has been interpreted differently throughout the country, with states such as Massachusetts and California, limiting compensation for egg donors to reimbursement for reasonable costs and direct expenses only. In New York, the Empire State Stem Cell Board, which administers funding for stem cells research, recently voted to compensate women up to $10,000 for egg donation.[56]

4.5 Research Resulting from the Licences Granted

During the period of operation of the Australian legislation, the Licensing Committee has issued 13 licences and is currently considering three licence applications. Of the licences issued, nine remain current.

Research currently conducted under Australian licences has resulted in an array of valuable outcomes. For example, under one licence, 21 disease-specific ES cell lines have been created and identified via pre-implantation genetic diagnosis as carrying a genetic disease.[57] These ES cell lines can be used for further differentiation and testing for a wide variety of purposes.

Other licences have been directed to developing culture media that are promising for improving outcomes for ART procedures and pregnancy success rates.[58]

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[56] Foohey P. (2010). *Paying Women For Their Eggs For Use In Stem Cell Research.* Pace Law Review 30(3) 900-926.

[57] Bradley CK et al. (2010). *Derivation of three new human embryonic stem cell lines. In vitro* Cellular & Developmental Biology – Animal 46(3-4): 294-299.

[58] National Health and Medical Research Council. (2010). *NHMRC Embryo Research Licensing Committee report to the Parliament of Australia for the period 1 March 2010 to 31 August 2010.*

Research conducted under another Australian licence has led to the development of successful tests to prevent recurrent miscarriages caused by chromosomal abnormalities.[59]

In addition, human ES cell lines derived under Australian licensed projects have been used extensively nationally and internationally in a broad range of research.[60]

Sydney IVF has recently derived four human ES cell lines from embryos identified as affected by Huntington's disease (HD). These HD-affected human ES cell lines will be used by laboratories nationally and internationally to further test and offer important foundations for investigating the fundamental aspects of this disease.[61]

4.6 National Stem Cell Centre and National Register of Donated Excess ART Embryos

The Australian Stem Cell Centre (ASCC) was established in 2002 and is an Australian Government funded organisation. ASCC is a dedicated funded body for stem cell research in Australia.[62] In addition, the ASCC assists in the creation and distribution of pluripotent stem cell lines, derived by iPS and ES cell techniques.

Through the Stemcore facility, the ASCC has distributed stem cell lines to researchers nationally and internationally for further research.

The ASCC has provided education programs to ensure Australian researchers seeking a career in stem cell research have the proper skills to conduct the research effectively.

The Australian Government will cease funding to this body as of the 30 June 2011 at which point monitoring and distribution of pluripotent stem cell lines throughout the country will no longer be available through this portal. However, the Australian Government has provided funding of $21 million to establish Stem Cells Australia at the University of Melbourne.

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[59] Jansen RPS et al: (2009). *Ovarian stimulation, blastocyst culture and preimplantation genetic screening for elective single embryo transfer.* In: Single Embyro Transfer, Gerris J, Adamson GD, De Sutter P, Racowsky C (editors). Cambridge University Press, Cambridge 93-108.

[60] Bradley CK et al. (2010). *Derivation of three new human embryonic stem cell lines.* In Vitro Cellular & Developmental Biology – Animal 46(3-4): 294-299.

[61] Bradley CK et al. (2011). Derivation of Huntington's Disease-Affected Human Embryonic Stem Cell Lines. Stem Cells and Development 20(3): 495-502.

[62] Department of Innovation, Industry, Science and Research. *The Australian Stem Cell Centre.* Retrieved from: http://www.innovation.gov.au/industry/biotechnology/australianStemCellCentre/Pages/default.aspx.

A national registry of donated excess ART embryos has not been established and submissions did not call for a registry. In the Committee's view, there is no apparent need within Australia to create one.

4.7 Consent: the Effectiveness of Legislative Provisions and NHMRC Guidelines

The overall response in submissions to the Review Committee is that legislative provisions and NHMRC guidelines relating to proper consent have been appropriate. There have been however, some key issues identified for consideration by the Review Committee.

4.7.1 Responsible Persons

A number of submissions raised an issue related to s 8 of the *Research Involving Human Embryos Act 2002.* Section 8 provides definitions of a 'responsible persons' in relation to donated material, which includes excess ART embryos, genetic materials and eggs.

The issue predominantly arises from the lack of clarity surrounding the concept of responsible person(s) in relation to the use of fetal tissue. Section 20(1)(d) allows applications for licences to generate human embryos from precursor cells from a human embryo or fetus. If a licence were granted, a responsible person would be required to give consent of the precursor cells from a human fetus.

Section 8 of the *Research Involving Human Embryos Act 2002* also lacks a definition of the responsible person(s) with respect to failed-to-fertilise eggs or abnormally fertilised eggs formed during ART. In these cases, the donated material is still an egg because it has not divided, but there may be genetic material from the father inside the egg that has not fused with the genetic material from the mother. Such failed-to-fertilise or abnormally fertilised eggs do not have the potential to develop into an embryo.

4.7.2 Limits on Number of Embryos Donated to Licensed Activities

A number of submissions addressed the issue of limiting numbers of embryos donated to licensed activities.

Responsible persons give consent for their excess ART embryos to be used in a specific research project. The embryos cannot be used for another project without going back to the responsible persons to request consent for that new project.

In its submission, NHMRC stated:

> The Licensing Committee has become aware that some licence holders are recruiting more embryo donors and consequently obtaining consent to store many more excess ART embryos than the number permitted to be used under licence. Consequently there may be significant numbers of donated but unused embryos in storage when the licence expires or the licensed activity terminates for some other reason. Standard Condition 4201 requires the licence holder to contact the responsible persons if their embryos remain unused at the end of a licensed activity and they have not already given written instructions regarding this situation. The options are to donate the embryos to another project if one is available or to allow the embryos to succumb.

When people make a decision to donate their excess ART embryos to a specific research project they expect that the embryos will be used for that project and in a reasonable time. They may be distressed to learn that their embryos were not used for the research to which they gave consent for. They may also be distressed at having to revisit a decision made, in some cases many years previously, and being asked to make a new decision about the fate of their embryos for a different research project.

4.7.3 Storage of Excess Embryos in the Absence of a Licensed Project

The Licensing Committee raised concerns that some clinics may be storing excess embryos even though there is no research project, or indeed any prospect of a research project, available to use the stored embryos.

For similar reasons as given above, the Licensing Committee considers this ethically undesirable and would welcome a strategy to prevent it happening. Such a strategy may involve cooperation between NHMRC and the Reproductive Technology Accreditation Committee of the Fertility Society of Australia.

4.8 The Range of Matters for Which the NHMRC Licensing Committee May Issue a Licence

4.8.1 'Significant Advance in Knowledge'

Section 21(4)(b) of the *Research Involving Human Embryos Act 2002* requires that Licensing Committee has regard to 'the likelihood of significant advance in knowledge or improvement in technologies for treatment as a result of the use of excess ART embryos or human eggs, or the creation or use of other embryos proposed in the application which could not reasonably be achieved by other means'.

As discussed in NHMRC's submissions, there has been ongoing debate between the Licensing Committee and applicants or licence holders on whether particular project proposals have the necessary scientific rigour to satisfy this requirement. However, as discussed below, the Review Committee does not consider that further legislative provisions would be helpful in this regard.

4.8.2 Role of Human Research Ethics Committee (HREC)

Section 21(3)(c) of the *Research Involving Human Embryos Act 2002* requires that before a licence can be issued the licence application must have been assessed and approved by a HREC 'that is constituted in accordance with, and acting in compliance with, NHMRC's *National Statement on Ethical Conduct in Research Involving Humans (1999)'*.

The current version of this document is the *National Statement on Ethical Conduct of Human Research (2007)* (the National Statement). The National Statement sets out ethical issues that should be considered by a HREC as it considers the ethical appropriateness of a research project, including those involving human embryos.

A HREC is not required to consider the matters that the Licensing Committee is required to consider, and this could lead to an institutional review that is not in the context of the regulation surrounding use of human embryos for research.

Further, there has been some suggestion that some HRECs have inadequate expertise or experience to consider research proposals involving human embryos. Possible alternative solutions are the establishment of a national HREC specialising in licensable activities or a system of accreditation.

The Review Committee considers that the latter would be more effective and efficient, and consistent with the National Statement. NHMRC has established a scheme for the certification of ethical review processes used in multi-centre human research and a similar scheme could be established for licensable activities.

4.9 Research or Clinical Practice which has been Prevented as a Result of Legislative Restrictions

The licensed research institutes in Australia have generally reported that the current legislation supports their research practices and no significant changes to the legislation are required.

However, two changes have been suggested in terms of allowing research that is currently restricted by the legislative provisions.

Section 20 (1)(e) of the *Research involving Human Embryos Act 2006* permits experimental fertilisation of human eggs and their study up to the point

where the egg divides into two cells (the first mitotic division). In order to identify and develop ART techniques, it has been suggested that the Licensing Committee authorise, by license, the ability to observe an experimentally fertilised egg through later stages of cell division.

Secondly, research into mitochondrial DNA disorders has been restricted or limited by s 10A (b)(ii) of the *Research Involving Human Embryos Act 2006* and s 13(b) of the *Prohibition of Human Cloning for Reproduction Act 2006* that prohibit the creating, developing or using an embryo containing genetic material provided by more than two persons.

A submission requested the Review Committee consider excluding mitochondrial DNA from the genetic material provided by more than two persons from the legislative provisions in order to allow further research into this disease. The use of eggs and embryos in research related to mitochondrial disease is complex, and is one of the issues the Review Committee considered in depth (see Section 5).

4.10 Licensing Committee's use of Information and Education to Assist Researchers; Legally Binding Rulings

There has generally been a positive response to the extent to which the Licensing Committee has effectively used information and education tools to assist researchers working in the field. A limited number of submissions address the issue.

Observations that were provided in regards to the effective provision of information and education tools include the following:

- Information provided on the NHMRC website is comprehensive but complicated. Information is not readily available or in a structured format.
- There is a gap in information about the breadth of the current legislation. The Australian Stem Cell Centre conducted a survey of several stem cell researchers and concluded that there seems to be a perception both in the general community and in scientific circles that these Acts form the 'stem cell legislation'. This has caused some difficulties for researchers who have requested approval from their institutional HREC to use existing human ES cell lines but experienced delays as the ethics committees seek clarification on the reach of the legislation to human ES cell lines.

No submissions were received about legally binding rulings.

It has been suggested that these issues could be addressed by:

- refining the National Statement on Ethical Conduct in Human Research (2007);
- maintaining and publishing a list of human ES cell lines that have been derived in a manner consistent with Australian regulations, similar to the NIH Human Embryonic Stem Cell Registry (see section 4.5);
- encouraging an ongoing education strategy to keep human research ethics committee members abreast of developments in the stem cell field; and
- introducing a web-based tool similar to the UK Stem Cell Toolkit which is 'intended to be a reference tool for those who wish to develop a programme of human stem cell research and manufacture, including clinical applications.[63]

4.11 Commonwealth/State Cooperation; Further Legislation.

A diverse array of responses were received regarding Commonwealth and State cooperation in the area of embryo research and the requirements for further Commonwealth or State legislation.

Some of those making submissions supported the current legislative framework and expressed the view that the Commonwealth and States cooperate well.

Those State Governments representatives who made submissions (New South Wales and Western Australia) did not make any substantial complaint about Commonwealth cooperation or cooperation between States. The Review Committee met representatives from the Victorian and New South Wales Government departments and representatives of the Office of the Chief Medical Officer from Western Australia and all supported legislation in its current form.

[63] Department of Health, UK. (2011). UK Stem Cell Tool Kit. Retrieved from: http://www.sc-toolkit.ac.uk/home.cfm.

5 ISSUES

Having considered the Terms of Reference and the submissions made to Review Committee, we now turn to the issues which have emerged. Unless otherwise indicated, the Review Committee's recommendations are unanimous.

5.1 Cloning for Reproduction

The Review Committee considers that cloning of a human being for reproduction contravenes the most basic understanding of human identity and individuality. No submission suggested that the legislative ban on human cloning for reproduction should be lifted, nor that there should be any change to any of the other criminal offences in the *Prohibition of Human Cloning for Reproduction Act 2002*.

> **Recommendation 1:** Cloning of a human being for reproduction should remain a criminal offence. The other criminal offences in the *Prohibition of Human Cloning for Reproduction Act 2002* should also remain.

5.2 Research on Human ES Cells

Research on human ES cells has already produced substantial benefits. Some detail will be found Section 4.2 above. To mention only a few, scientists at Sydney IVF have derived four human ES cell lines from embryos identified as affected by Huntington's disease. These cell lines will be made available to biomedical research laboratories and will provide a valuable tool to investigate both mechanisms and potential treatments of this severely disabling disease.[64]

Progress has been made in developing pancreatic cells from human ES cells to generate insulin-producing cells with the eventual aim to treat patients with juvenile onset diabetes.[65] Very recently there have been reports of early success in use of human ES cells in treatment for spinal cord injury.[66]

There remain many who contend that ethical concerns should still outweigh any benefits that might be derived for ES cell research. A numerical majority

[64] Bradley CK et al. (2011). Derivation of Huntington's Disease-Affected Human Embryonic Stem Cell Lines. Stem Cells and Development 20(3): 495-502.

[65] Kroon E et al. (2008). *Pancreatic endoderm derived from human embryonic stem cells generates glucose-responsive insulin-secreting cells in vivo.* Nature Biotechnology 26: 443 – 452.

[66] Stein R. (2011). *Stem cells were God's will, says first recipient of treatment.* Investor Stemcell. Retrieved from: http://investorstemcell.com/featured/stem-cells-were-god%E2%80%99s-will-says-first-recipient-of-treatment-by-rob-stein/.

(188) of submissions made to us, largely from individuals, were against human ES cell research.

The Review Committee considers that perhaps the best indicator of community attitude is that in 2002 and 2006 conscience debates in Commonwealth and State Parliaments resulted in statutory approval of human ES cell research, subject only to rejection by the West Australian legislature in 2006 with regard to SCNT research.

According to press reports, the Western Australian Government is currently considering amending legislation to bring it into line with the federal legislation and the legislation in other jurisdictions.

Judging by the total number of submissions received by us as compared with those received by the Lockhart Committee (264 to this review v 1,035 to the Lockhart Review), there may be increasing public acceptance of carefully regulated ES cell research over the recent decade.

Objectors to ES cell research argue that an embryo is human life and should not be deliberately destroyed, no matter how worthy the purpose of such destruction.

Against this is the reality most excess embryos from an ART procedure, typically 10-20 per couple,[67] are going to be deliberately discarded anyway. The ethical concern is perhaps not as problematic as in the case of SCNT where an embryo is created for the purpose of destruction for research.

The Academy of Science submission quoted the current Director of the United States National Institutes of Health, Dr Francis Collins, well known for his conservative Christian ethical views, as well as for his scientific research as a human geneticist, as saying:

> … not enough [is] yet known about [iPS] cells to guess whether they have the same therapeutic potential as embryonic stem cells. Will that matter for the therapeutic uses we all dream of? No one knows, but it would be foolish now to proceed without comparing them at every step to the gold standard for pluripotency – and that remains the human embryonic stem cell. So it's not 'either/or' that we should be pursuing. It's 'both/and'. 68

Nevertheless, an embryo must be the object of special consideration and respect, beyond that due to other human tissue. That need is in our opinion adequately met by the present legislation which mandates approval of any

[67] Williamson B. (2011). *Salvation in a cell*. The Australian Literary Review 6(4): 21

[68] Boyer PJ (2010) *The Covenant*. The New Yorker. Retrieved from: http://www.newyorker.com/reporting/2010/09/06/100906fa_fact_boyer?currentPage=all

proposed research by a well-qualified Licensing Committee, responsible to the Minister who is in turn responsible to Parliament, followed by ongoing Licensing Committee monitoring and inspection.

By international standards, Australia has a comparatively restrictive regime, as illustrated by the discussion in Section 4.4.

The fact that since 2002 there have been only 13 licences granted, of which three involve essentially the one project, suggests that there is a careful approach both from researchers seeking approvals, and the Licensing Committee granting licences.

> **Recommendation 2:** (by majority) Research involving embryos and ES cells should continue to be permitted subject to the statutory controls in the present legislation.

The foregoing represents a majority view of the Review Committee. Reverend Kevin McGovern, however, notes:

> Section 8 of the NHMRC *Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research* requires that embryos which must be disposed of should be disposed of respectfully. He does not believe that the evisceration of these embryos to extract their stem cells is respectful disposal. As we would be concerned if this was done to a human being at any other stage of human development, he believes that we should be concerned about this.

5.3 Somatic Cell Nuclear Transfer

All members of the Review Committee held concerns about the ethics of creating human embryos for destruction for use in research (and an SCNT created embryo, to be useful, must be an embryo with the full potential of any embryo) unless there were no other way that the outcome of the work could be achieved, and the potential outcome from the work was sufficient to benefit socially and to satisfy a utilitarian ethical argument that the work should be allowed.

While noting that there has not been much evidence to date that SCNT derived ES cells could be used to achieve outcomes not achievable by other means, the Review Committee recognised that it was not possible for anyone to predict what may occur in this area of research in the future.

The Review Committee therefore held that the legislation should be left as it is, permitting licensed SCNT experimental work. However, the Licensing Committee should be reminded that it should continue to ensure that any proposed project for which a licence is sought would satisfy a utilitarian ethicist's argument that the potential benefits of the work were sufficient

to justify overruling the legitimate moral concerns of some members of the community about the creation of embryos for destruction.

Many scientific submissions to the Committee (for example the Australian Academy of Science) stated that obtaining ES cells from patients with particular diseases could become a preferred method of generating cellular models for disease, both for research into the disease process and for drug testing. These 'disease-specific' stem cells can already be obtained by iPS cell technology, but there may be advantages for models derived from SCNT-derived stem cells as explained below.

SCNT could also be used in research into mitochondrial diseases. Instead of transferring the nucleus of a person's body cell into an enucleated donated egg, the nucleus of a fertilised egg would be transferred into an enucleated donated egg's cytoplasm. This would enable the nucleus from the egg of a couple at risk of having a child with mitochondrial disease to develop in the donated enucleated cytoplasm that has normal mitochondria, instead of the diseased mitochondria of the woman whose egg was first fertilised.[69]

In future, it may be possible to use SCNT-derived ES cells for therapy. That is not likely to happen for some years, if at all. However, there have been significant developments in research involving animal and human ES cells[70] and clinical trials for patients with spinal injury in the US have started to test the safety of ES cells derived from donated embryos.[71]

If these cells are shown to be safe and effective, and iPSC do not have the necessary properties, there may be increased interest in using SCNT-derived stem cells for this therapy as there would be less risk of them being rejected by the patient's immune system. The patient would not have to take immuno-suppressive drugs for the rest of his or her life. These drugs have their own side effects and risks. However, patients with serious spinal injury or other serious diseases may accept life-long immunosuppression and its risks.

To date, there has been little progress with SCNT in humans. Over seven years of research no researcher has claimed to derive human ES cells by SCNT,[72] though development of fetuses to the 8 cell stage has been achieved. Proponents of the work in Australia have argued that the lack of success to date is due to the required use of 'substandard' human eggs under the current

[69] Katsnelson A. (2010). Freeing human eggs of mutant mitochondria. Nature News. Retrieved from: http://www.nature.com/news/2010/100414/full/news.2010.180.html.

[70] Byrne J at el. (2007). *Producing primate embryonic stem cells by somatic cell nuclear transfer.* Nature 450:497–502.

[71] Geron Corporation. (2010). *ABOUT GRNOPC.* retrieved from: http://www.geron.com/GRNOPC1Trial/grnopc1-intro.html

[72] With the exception of work reported from Korea and later admitted to be fraudulent.

legislation. However, this limitation, while true in Australia, has not applied elsewhere, and overseas research has been no more successful.

Even with animal research, the progress has been slow. The value of human SCNT remains hypothetical until human ES cells can be derived from SCNT. Also, it is not know whether SCNT-ES or iPS cells will ultimately provide the better model in complex diseases where ES cells derived from donated embryos may be unavailable.

Since 2007, the new technology for developing pluripotent stem cells by induction of de-differentiation of somatic cells (iPS cells) has gradually become more sophisticated. Initially, retrovirus mediated genetic modification of the somatic cells was required but the same effect can now be achieved for both animal and human cells without this requirement.

These iPS cells are not identical to ES cells derived from surplus frozen embryos derived by *in vitro* sperm – egg fertilisation, as there are subtle epigenetic modifications to their genetic information. But functionally (from limited tests to date), optimal iPS cells carry the same potential as ES cells for tissue-specific differentiation *in vitro,* the ultimate goal of therapeutic cloning.

iPS cells, similarly to ES cells derived from SCNT, are matched to the person from whom they were derived, and therefore more likely to be usable to prepare tissue for organ repair or replacement than tissue derived from ES cells from an unrelated donor.

A number of submissions to the Review Committee suggested reasons for continuing SCNT with human cells, despite the development of iPS cells and other alternatives.

Although there are many technical difficulties in deriving human ES cells by SCNT, many scientists hypothesise that ES cells derived from SCNT are likely to more closely approximate the 'gold standard' of ES cells derived from ART than iPS cells. Further, they state that patient-specific ES cells whether derived by SCNT or iPS technology have potential advantages over ART-derived ES cells unrelated to the potential recipient.

When iPS cells were first developed, they were regarded by many scientists as being equivalent to ART-derived ES cells, and as providing the same potential for creating disease models for research and possible therapies.

Both types of stem cells are pluripotent and, it seemed, they could both provide patient-specific stem cells that would not be rejected by the patient.

However, a number of more recent publications[73] have suggested that there are significant differences between ART-derived ES cells and iPS cells:

- iPS cells, which necessarily come from patients after birth, may be imprinted with information that traces them back to their differentiated cell of origin (eg. a skin cell) or that information may come through the ageing of the person and their cells. In contrast, ART-derived ES cells are at an early stage of development. Data from animal-derived ES cells suggest that ES cells derived from either ART or SCNT may be more homogeneous than iPS cells, and have fewer problems with epigenetic imprinting.
- iPS cell lines as with ES cell lines derived from SCNT differ from one another even when they are derived using the same techniques and reagents, for reasons that are not yet clear. This may raise quality concerns if they are used in research as each batch of iPS cells would need to be independently verified to meet the requirements of quality assurance or regulatory authorities.

On the basis of experience to date, ART-derived ES cells are more likely to be consistent and stable over time. As Dr Andrew Elefanty, Monash University, said:

> There are significant issues concerning iPS cells relating to genetic stability, safety and their efficacy for generating the desired differentiated cells.[74]

Submissions to the Review Committee also suggested the possibility that SCNT-derived ES cells may have advantages over ES cells derived from ART embryos, as well as from iPS cells:

- Cells from donated embryos are more likely to be available for single gene Mendelian disorders such as Huntington's disease or cystic fibrosis, but are unlikely to provide models for those heritable diseases e.g. childhood diabetes where many gene variants contribute to risk, because embryos carrying the risk of these disorders cannot be reliably identified.
- ES cells derived from SCNT (or iPSC) would provide better disease models of late-onset conditions than ES cells derived from ART embryos.
- Because SCNT-derived ES cells (and iPS-derived ES cells) would be patient-specific, they would be less likely to be rejected by the patient's immune system if transplanted back to the donor. If cells from a donated embryo are transplanted into a patient, as in the first clinical trial involving human ES cells currently taking place in the US, the patient will possibly need to take immuno-suppressive drugs for the rest of life.

[73] Hayden E. (2011). *Reprogrammed cells trigger immune reactions in mice.* Nature News. Retrieved from: http://www.nature.com/news/2011/110513/full/news.2011.286.html.

[74] Dr Andrew Elefanty, Monash University*, with representatives from the Australian Stem Cell Centre, – verbal presentation to the Legislation Review Committee on 18 April 2011*

In summary, it is not know at this stage, which type of stem cell research will ultimately be most productive. As Dr Megan Munsie from the Australian Stem Cell Centre said in an additional submission to the Review Committee:

> It will be difficult to assess the potential use of SCNT-derived stem cells until they have in fact been derived in humans. However, SCNT-ES cells are still seen as more closely resembling (ART derived) ES cells than iPS cells. There was a recent paper in Nature (Kim et al (2010) 467, 285-290) that compared mouse ES cells generated by SCNT, from an embryo and iPS cells derived from fibroblasts and blood cells. This paper demonstrated that reprogramming with transcription factors can leave an epigenetic memory mark in iPS cells reminiscent of the donor cell type. In an accompanying commentary (Zwaka (2010) Nature 467:280-1), it was stated that 'Ultimately, it seems as though we have different reprogramming tools on hand that produce slightly different pluripotent stem cells. Rather than asking which of these tools is likely to yield superior results, the focus should be on the most appropriate application for each method. It must be kept in mind, however, that authentic ESCs remain the gold standard against which all reprogramming technologies must be judged'. … However, I have to acknowledge that there were technical variations in methodology (inhibitors in some culture media and not in others) that may have influenced the reprogramming state (this is discussed in a review by Hanna et al 2010 Cell 143:508-25).

Similarly, Professor Bob Williamson, President of the Australian Academy of Science, said in the Academy's submission;

> The usefulness of SCNT-derived cells therefore revolves around two issues. The first is that there are many diseases which are late-onset, and are not Mendelian although they have a genetic component. Among the diseases in this group are Alzheimer's, Parkinson's, MND, and many cancers. There are no PGD-derived 'unfit for transfer' embryos, because there are no prenatal tests available and because the diseases are late-onset. These are common diseases that are important causes of health burden. They are particularly important to study, in terms of cellular models of disease. The second is that we do not know what the implications of many aspects of stem cell-ness are for safety. We know that ES cells can (but do not always) form teratoma and teratocarcinoma. We know that imprinting will limit the ability of a cell to differentiate into all cell types, and may also be involved in either allowing or preventing tumour formation. We know that SCNT cells differ from both ES cells and iPS cells.

Given the uncertainty about future outcomes, many scientists and others believe that both types of research should be pursued.

With regard to 'proof of concept' in animal research, there have been very few papers that have discussed this in relation to SCNT. However, there have been some apparent successes.

In a study published in 2002, a group in the US temporarily corrected a blood disease in a mouse by combining SCNT-ES with gene therapy[75]. However, the transplanted cells were later rejected for immunological reasons so disease prevention could not be established.

A study published in 2008 showed that SCNT-ES cell lines from Parkinsonian mice showed therapeutic efficacy and lack of immunological response when transplanted into individually matched host mice.[76]

With regard to community attitudes to SCNT, there have been a number of surveys on community attitudes regarding embryo and stem cell research that have been mentioned in Section 4.3. As often happens, some surveys are open to criticism concerning the implicit assumptions or context of the questions and the analysis of the answers. However, the most recent surveys suggest that the majority of the Australian community supports stem cell research even where it involves donated human embryos and therapeutic cloning (SCNT).

The Review Committee received many submissions regarding the ethical issues raised by use of SCNT. Most of these stated that all human embryo research is morally objectionable and that creating an embryo for research is morally worse than using 'excess' embryos from fertility treatment programs where those embryos must otherwise be destroyed if they are not donated to another couple or used in research. Some argued that ART-derived ESC are 'here to stay' although not really acceptable, whereas SCNT work is unjustified on current knowledge.

There were also many submissions from those who support SCNT research, including moving personal presentations by four patient representatives who were members of CAMRA (Coalition for the Advancement of Medical Research Australia).

The Lockhart Committee decided early in its deliberations not to adopt any single normative theory or aspect of 'principlism' … [but, instead] to adopt an approach based upon fundamental (shared) moral values, an acceptance of pluralism and diversity in community(s) and on processes of deliberative democracy.[77]

This approach was advised by the ethicist on the Lockhart Committee, Dr Ian Kerridge, who also described it as 'an approach of pragmatic discourse,

[75] Hayden E. (2011). *Reprogrammed cells trigger immune reactions in mice.* Nature News. Retrieved from: http://www.nature.com/news/2011/110513/full/news.2011.286.html.

[76] Tabar et al. 2008. Therapeutic cloning in individual Parkinsonian mice. *Nature Medicine 14: 379–381.*

[77] *Skene L et al.(2008). The Lockhart Committee: Developing Policy through Commitment to Moral Values, Community and Democratic Processes* Journal of Law and Medicine 6(1):132-138.

or communicative morality, similar to that described by Habermas'; he said that it would help 'find a way to reconcile the inevitable conflicts inherent in pluralism and liberal democracy'.[78] A primary shared value observed by the Review Committee was to assist patients with serious medical conditions.

Many submissions to the Review Committee also mentioned the extensive community consultation process undertaken before the Federal legislation was passed in 2002, during the deliberation of the Lockhart Committee and during the Parliamentary process when the Lockhart Committee's recommendations were almost entirely adopted in legislative amendments.

The New South Wales and Victorian Government representatives also told the Committee about the consultation process accompanying the introduction and amendment of the State legislation.

These State Government representatives did not believe that the views of the general community in their jurisdictions have changed despite scientific developments since the legislation was last reviewed. They said that the provisions regarding embryo research and SCNT should not be amended.

Thus, the Review Committee has noted the profound concerns that have been expressed about embryo research, particularly SCNT, in many submissions it has received and the concerns have been very carefully considered.

However, the Review Committee has also considered the possible, future benefits of human ES cell research. The current legislation and other regulatory provisions allow this research to be undertaken only under licence and ethical oversight, described below.

These constraints take account of concerns about embryo research by imposing strict controls on the circumstances in which human embryos may be used in research and they limit the number of embryos to those that are necessary to achieve significant results.

The Review Committee noted that there are many controls in the current legislation and the wider regulatory system that provide stringent oversight for all human embryo research in Australia.

Many activities are prohibited by the legislation with substantial criminal penalties for breach. Examples of these statutory offences include human cloning for reproduction, combining human and animal gametes (sperm and eggs) to breed hybrids, allowing a human research embryo to develop longer than 14 days; and the sale of human eggs.

[78] ibid

Undertaking SCNT without a licence is a specific statutory offence under s10A of the *Research Involving Human Embryos Act 2002*.

There are strict controls on the Licensing Committee in considering applications for a licence. In particular, s 21 of the *Research Involving Human Embryos Act 2002* states that:

> (3) The NHMRC Licensing Committee must not issue the licence unless it is satisfied of the following:
>
> (a) that appropriate protocols are in place:
>
> (i) to enable proper consent to be obtained before an excess ART embryo or human egg is used, or other embryo is created or used under the licence (see paragraph 24(1)(a)); and
>
> (ii) to enable compliance with any restrictions on such consent;
>
> (b) if the use of an excess ART embryo proposed in the application may damage or destroy the embryo—that appropriate protocols are in place to enable compliance with the condition that such use is authorised only in respect of an embryo created before 5 April 2002 (see subsection 24(3));
>
> (c) that the activity or project proposed in the application has been assessed and approved by a HREC that is constituted in accordance with, and acting in compliance with, the NHMRC National Statement on Ethical Conduct in Research Involving Humans (1999), as in force from time to time.
>
> (4) In deciding whether to issue the licence, the NHMRC Licensing Committee must have regard to the following:
>
> (a) restricting the number of excess ART embryos, other embryos or human eggs, to that likely to be necessary to achieve the goals of the activity or project proposed in the application;
>
> (b) the likelihood of significant advance in knowledge or improvement in technologies for treatment as a result of the use of excess ART embryos or human eggs, or the creation or use of other embryos, proposed in the application, which could not reasonably be achieved by other means;
>
> (c) any relevant guidelines, or relevant parts of guidelines, issued by the CEO of the NHMRC under the *National Health and Medical Research Council Act 1992* and prescribed by the regulations for the purposes of this paragraph;
>
> (d) the HREC assessment of the application mentioned in paragraph (3)(c);
>
> (e) such additional matters (if any) as are prescribed by the regulations.

In addition to the statutory, licensing, reporting and ethics committee constraints on human SCNT research in Australia, there are constraints in science itself.[79] Some of these were mentioned by representatives of the Victorian Government in their personal presentation to the Review Committee (5 May 2011):

- SCNT has proved technically difficult (237 eggs were used in the SCNT process of creating Dolly the sheep); and despite the theoretical benefits that have been suggested by some scientists, no human stem cell lines have been derived by SCNT.
- SCNT would require human eggs to be donated for research and there are likely to be very few human eggs available, noting that it is unlawful in Australia to use animal eggs with human somatic cells for SCNT.
- The eggs that have been available for research are not 'full healthy oocytes' (Sydney IVF) and are therefore not optimal for use in research.
- There are currently other forms of research that appear more likely to be productive. For example, there have been many developments in adult stem cell research, cellular reprogramming and the discovery of iPS cells and, at present; these seem to present greater opportunities for new research.
- In order to obtain a licence to undertake SCNT research, scientists must first obtain ethics approval. This takes time and considerable documentation and the outcome of a licence application is uncertain.
- It is clearly unlawful under the present legislation for any research involving human embryos to be undertaken without a licence from the Licensing Committee (see above), or in contravention of the conditions of a licence. In order to obtain a licence, the applicant must make a good case for being allowed to do the research. In a contentious area like SCNT, this would involve a particularly rigorous evaluation of the applicant's arguments on why the proposed research should be done, and the likelihood that it will be successful (on the basis of animal research; research in other countries etc). The Licensing Committee would consider these issues thoroughly and critically before granting a licence.

[79] In the UK, the creation of 'admixed human embryos' (human-animal embryos) using eggs from cows to obtin human stem cells for research is lawful. However, by 2011, none of that research has been funded despite the regulation being in place to allow it and it is therefore not being undertaken.

- The Licensing Committee cannot grant a licence unless it is satisfied that 'the number of embryos or human eggs [is restricted] to that likely to be necessary to achieve the goals of the activity or project proposed in the application' and that there is a 'likelihood of significant advance in knowledge or improvement in technologies for treatment as a result of the creation or use of other embryos, proposed in the application, which could not reasonably be achieved by other means': Research Involving Human Embryos Act 2002 s 21 (3). This will be difficult to establish when the science involving SCNT is at such an early stage.
- Whether proposed research is undertaken for commercial reasons or as part of research funded by a government funding agency, results will be expected in a fairly short time frame. For example, research grants are commonly for three years and the results of research in the early part of the grant will be expected to support an application for later funding. It is unlikely that any results from SCNT could be obtained in such a short time, if at all.

The Review Committee notes the significant ethical concerns that have been expressed about research involving SCNT in humans in many of the submissions it has received.

Because of the lack of progress of animal and human SCNT research to date, there is a more rigorous standard related to 'a real likelihood of a significant advance that researchers, that could not be reasonably achieved by other means' that should be met in order for the Licensing Committee to issue a licence.

> **Recommendation 3:** (by majority) The provisions in the current legislation regarding SCNT should not be amended.
>
> However, in reaching this recommendation, the Review Committee notes the lack of progress in SCNT research in animals and humans. The Review Committee believes that this must impact on the Licensing Committee's interpretation of its statutory obligation, when it is considering any future application for a licence to undertake research involving SCNT, to take into account 'the likelihood of significant advance in knowledge or improvement in technologies for treatment as a result of the use of excess ART embryos or human eggs, or the creation or use of other embryos, proposed in the application, which could not reasonably be achieved by other means' when it is considering any future application for a licence to undertake research involving SCNT.

The foregoing represents a majority view of the Review Committee. Reverend Kevin McGovern, however, notes:

> the approach recommended by the Lockhart Review, which stated that 'the greater the potential benefits of an activity, the greater the need for ethical objections to be of a high level and widely accepted in order to prevent that activity. Conversely, where benefits are not yet established, or where there is widespread and deeply held community objection, then total prohibition through the legal system may be justified.' Reverend McGovern believes that in 2011 the latter standard has been reached for SCNT. In 2006, SCNT seemed the only way to seek the benefits of regenerative medicine. With the advent of induced pluripotent stem cells, this is no longer the case. It is hard to see what SCNT now contributes to the progress of regenerative medicine. What would be lost if Australia's regulatory regime permitted the harvesting of embryonic stem cells from excess embryos along with research with adult stem cells and induced pluripotent stem cells, but did not permit SCNT? Some scientists have proposed some possible benefits of SCNT, but their arguments are not entirely convincing. Dr Megan Munsie argues that SCNT-ES cells might more closely resemble ES cells than iPS cells. However, the evidence from animal work is that SCNT generally produces damaged or abnormal embryos. This strongly suggests that even if SCNT-ES cells more closely resemble ES cells, these SCNT-ES cells will still be genetically abnormal and inferior to ES cells. Professor Bob Williamson advocates SCNT to generate stem cell lines as disease models to study late-onset conditions. It is not clear, however, why SCNT-derived lines would be more useful than iPSC-lines. Beyond that, there is only the possibility of what 'might' be learnt if research into SCNT continues. The proposed benefits of SCNT research therefore seem not entirely convincing, sometimes rather small, and largely theoretical. On the other hand, SCNT involves the most profound of ethical concerns. It is the creation of human life which will be used in research and then destroyed. When people understand this, many people within the community are troubled by SCNT.
>
> For all this, however, this most serious of ethical concerns has been judged less significant than the mostly theoretical benefits which might come if research into SCNT is allowed to continue. With this outcome, Reverend McGovern wonders whether the ethical concerns about SCNT research are ultimately being given anything more than lip-service.

Dr Faye Thompson shares Reverend McGovern's concerns about SCNT.

> Dr Thompson supports Recommendation 3 on the basis that the Licensing Committee place emphasis on 'the likelihood of significant advance in knowledge or improvement in technologies for treatment as a result of the use of excess ART embryos or human eggs, or the creation or use of other embryos, proposed in the application, which could not reasonably be achieved by other means' when it is considering any future application for a licence to undertake research involving SCNT'.

5.4 Use of Excess ART embryos

The *Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research* (ART Guidelines) state that potential donors, 'responsible person(s)' of access embryos from IVF, after considering sufficient information, may consent to their IVF embryos being used for research. Potential donors are provided with a fixed period of time during which they may reconsider their decision. This 'cooling off' period is normally at least two weeks.[80]

Due to the 'cooling off' period all excess embryos from IVF, which have been donated for research, would be frozen, however s 24(8) of the *Research Involving Human Embryos Act 2002* allows for the Licensing Committee to modify, for the purpose of a license, this 'cooling off' period:

> (8) For the purposes of applying the condition referred to in paragraph (1)(a):
>
> (a) a licence may provide that the guidelines referred to in the definition of ***proper consent*** apply in a modified form in relation to the use, under the licence, of excess ART embryos that are unsuitable for implantation; and
>
> (b) if a licence so provides, the guidelines as modified by the licence have effect in relation to the giving of consent for such creation or use.
>
> Note: For example, the guidelines could apply to a particular licence in a modified form, to alter the cooling-off period required in relation to the use of excess ART embryos that are unsuitable for implantation.

On another matter, Sydney IVF suggested that, in order to identify and develop better ART techniques, the legislation be amended so that the Licensing Committee could authorise, by license, the ability to observe an experimentally fertilised egg through later stages of cell division. Currently, s 20 (1)(e) of the *Research involving Human Embryos Act 2006* permits experimental fertilisation of human eggs and their study only up to the point where the egg divides into two cells (the first mitotic division).

The Committee does not support the concept of training and research using embryos in later stages of cell division.

> **Recommendation 4:** The provisions in the current legislation regarding the cooling-off period related to the use of excess ART embryos for research should not be amended.

[80] National Health and Medical Research Council. (2007). *Ethical Guidelines on the use of Assisted Reproductive Technology in Clinical Practice and Research* s17.19

Recommendation 5: There should be no changes to the legislation that would permit research on embryos later than the point where the egg divides into two cells (the first mitotic division).

5.5 Payment for Egg Donation

Section 21 of the *Prohibition of Human Cloning for Reproduction Act 2002* presently provides:

> (1) A person commits an offence if the person intentionally gives or offers valuable consideration to another person for the supply of a human egg, human sperm or a human embryo.
>
> Maximum penalty: Imprisonment for 15 years.
>
> (2) A person commits an offence if the person intentionally receives, or offers to receive, valuable consideration from another person for the supply of a human egg, human sperm or a human embryo.
>
> Maximum penalty: Imprisonment for 15 years.
>
> (3) In this section:
>
> '***reasonable expenses***':
>
> (a) in relation to the supply of a human egg or human sperm--includes, but is not limited to, expenses relating to the collection, storage or transport of the egg or sperm; and
>
> (b) in relation to the supply of a human embryo:
>
> (i) does not include any expenses incurred by a person before the time when the embryo became an excess ART embryo; and
>
> (ii) includes, but is not limited to, expenses relating to the storage or transport of the embryo.
>
> '***valuable consideration***' , in relation to the supply of a human egg, human sperm or a human embryo by a person, includes any inducement, discount or priority in the provision of a service to the person, but does not include the payment of reasonable expenses incurred by the person in connection with the supply.

There is general acceptance in Australia of the principle that donation of human tissue should be altruistic. In the context of donation of embryos, anything else would be particularly open to the risk of exploitation. In the US substantial financial inducements can be offered.

The process for a woman donating eggs is intrusive and not particularly pleasant. It involves medication that has a hormonal effect over about ten days and hospitalisation for about half a day.

The present interpretation of *'reasonable expenses'* applied in practice involves out of pocket expenses such as medical and hospital expenses and taxi fares. It does not extend to loss of income. The assessment and payment of expenses is handled by the clinic concerned.

The Review Committee does not see any need for change, legislative or otherwise, to this system. It seems to work reasonably well. Certainly there were no public submissions in favour of compensation extending beyond 'reasonable expenses'.

The Review Committee does not favour extending the concept of reasonable expenses to cover loss of income. In the great majority of cases the amount involved would be small. As representatives of the Victorian Government pointed out, such an extension would create a precedent that would raise issues in other areas of tissue donation.

The Review Committee does not think it necessary to complicate the legislation by further defining reasonable expenses.

> **Recommendation 6:** There should be no change to s 21 of the *Prohibition of Human Cloning for Reproduction Act 2002* in relation to the payment of 'reasonable expenses'.

5.6 DNA from more than Two Persons and Research into Mitochondrial Diseases

Section 10A of the *Research Involving Human Embryos Act 2002* presently provides:

> A person commits an offence if:
>
> (a) the person intentionally uses an embryo; and
>
> (b) the embryo is:
>
> (i) a human embryo created by a process other than the fertilisation of a human egg by a human sperm; or
>
> (ii) a human embryo created by a process other than the fertilisation of a human egg by a human sperm that contains genetic material provided by more than 2 persons; or
>
> (iii) a human embryo created using precursor cells taken from a human embryo or human fetus; or
>
> (iv) a Hybrid embryo; and
>
> (a) the use by the person is not authorised by a licence.
>
> Maximum penalty: Imprisonment for 5 years

Section 13 of the *Prohibition of Human Cloning for Reproduction Act 2002* presently provides:

> A person commits an offence if:
>
> (a) the person intentionally creates or develops a human embryo by a process of the fertilisation of a human egg by a human sperm outside the body of a woman; and
>
> (b) the human embryo contains genetic material provided by more than 2 persons.
>
> Maximum penalty: imprisonment for 15 years.

Section 23 of the *Prohibition of Human Cloning for Reproduction Act 2002* also presently provides:

> A person commits an offence if:
>
> (a) the person intentionally creates or develops a human embryo by a process other than the fertilisation of a human egg by a human sperm; and
>
> (b) the human embryo contains genetic material provided by more than 2 persons; and
>
> (c) the creation or development of the human embryo by the person is not authorised by a licence.
>
> Maximum penalty: Imprisonment for 10 years.

Some submissions called for the ability to conduct further research by using DNA from more than two individuals to explore disorders involving mitochondrial DNA. Recent research using primate and human embryos in culture has indicated that the transfer of nuclear DNA from an affected embryo into a donated egg with its nucleus removed could possibly prevent inheritance of mitochondrial DNA disease.

It is an offence to create an embryo using genetic material from three persons, but only if the embryo is created by way of fertilisation. If the nucleus of a fertilised egg is transferred into an enucleated unfertilised donated egg from a third party, creating an embryo with genetic information from three donors by SCNT, there is currently no offence if this is done under licence.

However, creation of an embryo with mitochondrial DNA derived from a donor unrelated to the sources of the nuclear DNA could be a licensable activity for research purposes, so long as the embryo is not developed outside the body of a woman for more than 14 days and is not derived by way of fertilisation. This indicates that a licence could be granted to create an embryo

for no more than for 14 days, containing genetic material provided by more than two persons, by way of a technique similar to SCNT.

Researchers are suggesting that amendments be made to the legislation to permit the licensing of the creation of an embryo by way of fertilisation of an egg with human sperm from the DNA of more than two people up until the blastocyst stage. This amendment would assist further research on mitochondrial disorders

Mitochondria are small structures found in the cytoplasm of human cells that enable the process in which molecules from food are converted into high-energy molecules. They are essential for functions such as cell reproduction, transportation of materials, and protein synthesis.

Mitochondrial disorders are a group of diseases caused by damage to small structures found in human cells called mitochondria that are essential for cellular functions such as cellular reproduction, transportation of materials, and protein synthesis. These cells also support a process where food molecules are converted into high-energy molecules. The energy produced by mitochondria is essential for cellular and high functions. Mitochondrial disorders are genetically passed on from mothers to their children.

Inherited mitochondrial disorders are rare, debilitating and sometimes lethal. There is currently no cure. One set is due to faulty genetic information in mitochondrial DNA, which is inherited by a child solely from its mother, although not all offspring of a mother with a genetic disorder of her mitochondrial DNA will be equally affected. The symptoms of mitochondrial disorders are diverse, progressive and include loss of motor control, liver disease, visual or hearing loss and intellectual impairment. Between 200 and 300 Australian families are affected by these disorders.[81]

Recently, research in Newcastle, United Kingdom, described in *Nature*, has produced results with fertilising eggs and sperm from two couples, forming the donor and recipient zygotes (an early embryo) respectively. Later, the nucleus from one fertilised egg was removed at a pronuclear stage and transferred into the other fertilised egg whose nucleus had also been removed, at the pronuclear stage.

In that second step, the zygote that was 'treated' then contained genetic material from more than two people, but the resultant embryo was not created 'by

[81] Advanced Cell Technology (2010). *ACT Files European Clinical Trial Application for Phase 1/2 Study Using Embryonic Stem Cells to Treat Macular Degeneration,* retrieved from: http://www.advancedcell.com/news-and-media/press-releases/act-files-european-clinical-trial-application-for-phase-12-study-using-embryonic-stem-cells-to-treat-/.

a process of the fertilisation of a human egg by a human sperm'.[82] None of the steps in the research would be deemed to be unlawful in Australia under licence, provided they did not contravene other provisions of the legislation.

However, researchers argue that without the option of transferring the nucleus of a fertilized egg into a donated egg from which the nucleus has been removed, Australian families affected by mutations of mitochondrial DNA cannot be helped to have disease-free children. The alternative for these families is to use donated eggs and this would not involve any of the mother's genes, removing her genetic endowment to her children.

It has been submitted that further research into related techniques would be allowed if the legislation, s 10A (b) (ii) of the *Research Involving Human Embryos Act 2002* and s 13 (b) of the *Prohibition of Human Cloning for Reproduction Act 2002*, was amended to exclude mitochondrial DNA from the current description of 'genetic material provided by more than two persons'.

In light of the recent developments in mitochondrial research, the UK Human Fertilisation and Embryology Authority (HFEA) recently undertook a review into the usability and performance of the techniques that alter the mitochondrial DNA of an egg or embryo, to be used in assisted conception to prevent the transmission of serious mitochondrial diseases.

The HFEA introduced a provision in the 2008 amendment to the *Human Fertilisation and Embryology Act 1990* in order for the Government to have the power to assess the safety and effectiveness of the scientific procedures involved in the alteration of mitochondrial DNA. If the techniques were deemed safe and effective, legislation may be altered to permit the creation of an embryo by way of egg and sperm fertilisation for possible implantation using these techniques.

The HFEA agreed, in February 2011, to a request from the Secretary of State for Health to scope *'*expert views on the effectiveness and safety of mitochondrial transfer*'*. The Authority established an expert panel, with broad-ranging expertise, to collate and summarise scientific evidence submitted from a wide range of experts in the field.[83]

The expert panel presented its finding to the UK Department of Health on 18 April 2011 and made several recommendations regarding the effectiveness and safety of the current techniques used through the United Kingdom and internationally. One of the recommendations included:

[82] Tachibana M. et al. (2009). *Mitochondrial gene replacement in primate offspring and embryonic stem cells*. Nature 461: 367-372.

[83] Human Fertilisation and Embryology Authority. (2011). *Review of scientific methods to avoid mitochondrial disease*. Retrieved from: http://www.hfea.gov.uk/6372.html.

Although potentially useful clinical techniques, further safety experiments need to be done before introducing them into clinical practice.[84]

The Review Committee have taken into consideration the evidence and advice presented to us by Australian researchers wishing to undertake research into mitochondrial DNA disorders.

The Review Committee understands that in the future these techniques could be useful in preventing the transmission of mitochondrial DNA disorders and in regenerative medicine therapies. However, at this present point in time, the Review Committee does not believe these techniques are sufficiently advanced to be permitted under the current legislation.

> **Recommendation 7:** (by majority) There should be no change to the current legislation in relation to the use of DNA from more than two persons.

The foregoing represents a majority view of the Review Committee. Reverend Kevin McGovern, however, notes:

> If the current legislation does permit the creation of embryos through SCNT in an attempt to prevent the transmission of mitochondrial disease, Reverend McGovern argued that the legislation should be changed to exclude this. From the evidence given to the Review Committee, he was convinced that this proposed therapy could not be used for human beings not just in the short term but for the foreseeable future. The proposal to do this, therefore, is in his opinion simply hype – and, indeed, hype which might give false hope to some affected individuals. With genetic counselling, a woman with mitochondrial disease who does not wish to have an affected child might choose not to have children. Some others might choose to have a child through fertilising a donated egg (perhaps from one of their unaffected relatives) with their partner's sperm. While this child will not be the biological offspring of the affected woman, he or she will almost certainly be healthy. By contrast, this proposed technique is still unproven and inherently risky. Even to consider using it is, in Reverend McGovern's opinion, to focus far too much on the wishes of prospective parents and simply to ignore the rights of the child. Further, while scientists admit that much more work needs to be done to understand the interaction of mitochondrial and nuclear DNA. Reverend McGovern is also concerned that any such therapy might compromise the right of the child to be conceived with a natural biological inheritance.

[84] Human Fertilisation and Embryology Authority. (2011). *Scientific review of the safety and efficacy of methods to avoid mitochondrial disease through assisted conception* page 20 of 45.

5.7 Operation of the Licensing System and Human Research Ethics Committees

While some researcher groups expressed concern about the time needed to obtain a licence, most submissions which addressed the licensing system were broadly supportive of it.

For example, in its submission the ASCC recommended that the 'current national regulatory framework which oversees the responsible use of human embryos in Australian research should continue without significant change'. Indeed, 'the ASCC does not see any evidence that research or clinical practice in Australian stem cell science has been hindered by the current regulatory framework'.

In the same way, the submission from the Australian Academy of Science noted that for experiments involving the responsible use of human embryos, 'it is accepted that rigorous scrutiny (that may take time) is appropriate'.

In its submission, NHMRC noted how important it is that 'an application for the use of human embryos in research should be considered by an HREC that has appropriate knowledge and expertise in this area.' Thorough ethical assessment by appropriately qualified HRECs might even facilitate the work of the Licensing Committee.

NHMRC notes that one possible way to ensure this would be 'the establishment of a single, independent, national HREC to consider embryo research applications.' The Review Committee, however, were concerned that this might simply add another layer of national bureaucratic assessment which may further slow the process of approval of research involving human embryos.

Another suggestion by the NHMRC is 'credentialing HRECs that consider embryo research applications, to ensure that these have a high level of technical and ethical expertise.' NHMRC has recently undertaken a similar process through the Harmonisation of Multi-centre Ethical Review certification scheme, which assessed and certified a number of HRECs as being able to undertake single ethical review of multi-centre human research.

The Review Committee thought that this was a more realistic proposal. It allows research institutions to decide whether they want to continue to develop and resource their own institutional HREC to assess research involving human embryos, or whether they will enter into some cooperative arrangement with another institution whose HREC is credentialed to assess research involving human embryos.

This approach also allows NHMRC to assess regularly the expertise and resourcing of HRECs credentialed to consider research involving human embryos, and thereby to ensure that ethical assessment of these proposals is indeed undertaken by a HREC with appropriate expertise and resourcing.

NHMRC's submission raises a number of questions about what this system of credentialing should involve. The Review Committee does not wish to offer an opinion on these questions, but instead suggests that these matters be determined by AHEC and NHMRC in consultation with the Licensing Committee and other relevant stakeholders.

> **Recommendation 8:** The current framework for research involving human embryos which involves ethical assessment by a Human Research Ethics Committee and assessment of applications for licenses by the Licensing Committee should continue.
>
> **Recommendation 9:** In consultation with the Licensing Committee and other relevant stakeholders, AHEC and NHMRC should establish a system of credentialing for HRECs that consider research involving embryos.

5.8 Precursor Cells

Several submissions received by the Review Committee called for the repeal of s 20(1)(d) of the *Research Involving Human Embryos Act 2002.* This permits under licence the 'creation of human embryos using precursor cells from a human embryo or a human fetus, and use of such embryos.' Those who made this request included Australians for Ethical Stem Cell Research, the Life, Marriage and Family Centre of the Catholic Archdiocese of Sydney, and the Coalition for the Defence of Human Life.

The Review Committee recognises that some – perhaps many – people within our community experience the 'yuck factor' when they first consider this matter. Scientists do not currently know how to develop mature eggs from these precursor cells, or even if this is possible.

If it is indeed possible, the embryos created from these eggs will only be used for research and not be used for reproduction. Section 14 of the *Prohibition of Human Cloning for Reproduction Act 2002* forbids developing any human embryo outside the body of a woman for more than 14 days. It imposes a maximum penalty of fifteen years' imprisonment if this law is broken.

Further, s 20(3) of the same Act forbids the placing of an embryo created using precursor cells from a human embryo or foetus into the body of a woman. It also imposes a maximum penalty of fifteen years' imprisonment if

this law is broken. Therefore there is no prospect of a child becoming aware that he or she is derived from a deceased fetus.

The Review Committee is sensitive to the ethical concerns surrounding the creation, use and then destruction of human embryos. However, existing Australian law has judged that some embryo research is justified by the promise of regenerative medicine to cure serious diseases. In recognition of these ethical concerns, this sort of research can only be undertaken under licence, and the Licensing Committee must consider that this research holds promise of a significant advance in knowledge or an improvement in treatment technologies that could not reasonably be achieved by other means.

The Licensing Committee must also restrict the number of embryos used to that likely to be necessary to achieve the goals of this research. Not every Australian agrees with this position. However, with this legislation in place, it is difficult to see how the use of precursor cells from a deceased foetus *ex utero* could constitute an exceptional case.

The law permits women to donate their own eggs for use in Assisted Reproductive Technology or in research. With the informed consent of each responsible person, the *Research Involving Human Embryos Act 2002* permits the donation of excess embryos for research.

Chapter 4.1 of the *National Statement on Ethical Conduct in Human Research* permits the mother of a deceased fetus *ex utero* (along with anyone else whom she wishes to involve) to give consent for the use of tissue from that foetus in research. Given all this, it is difficult to see how an exception could reasonably be made to forbid the donation by each responsible person of precursor cells from a deceased foetus *ex utero.*

> **Recommendation 10:** Section 20(1)(d) of the *Research Involving Human Embryos Act 2002* should remain unchanged, permitting under licence the creation and use for research purposes of human embryos using precursor cells from a human embryo or a human fetus.

5.9 IVD Gametes

In its submission, NHMRC recommended that 'consideration be given as to whether research using IVD gametes should be permitted under licence and whether reproductive uses of IVD gametes should be permitted or prohibited'. Elsewhere in the same submission, NHMRC also recommended certain legislative changes if the reproductive use of IVD gametes is to be prohibited.

The Review Committee notes that at present the use of IVD gametes for reproduction remains theoretical. It is not known if it is even possible.

The Review Committee considers that certainly nothing is known about the reliability or safety of the use of IVD gametes. Even if community standards support this technology, our society would have to be very confident of the reliability and safety of this technology before the use of IVD gametes in human reproduction could be permitted.

Scientific progress with IVD gametes is discussed in Section 4.1.4 of this report. Mice have been produced using mouse IVD gametes. It is unclear whether functional human IVD gametes have yet been produced.

Where one partner or both is not producing gametes, human IVD gametes could be used to enable a heterosexual couple to have a child. If opposite-sex IVD gametes (an egg from a male or a sperm from a woman) could be produced, this technology might also enable a same-sex couple to have a child who is biologically theirs.

Further, this technology might also enable one person to have their own child without another parent through the fertilisation of his or her natural gamete with an opposite-sex IVD gamete derived from the same person. In all these examples, a male couple or individual would of course require the assistance of a surrogate.

The Review Committee recognises that community standards should determine whether the use of IVD gametes should be permitted in Australia. The Review Committee also think that the community has so far had little opportunity to consider this matter.

Among other human rights which she proposes for children in this age of reproductive technology, ethicist Margaret Somerville proposes a right 'to be conceived with a natural biological heritage' – that is, 'a right to be conceived from a natural sperm from one identified, living, adult man and a natural ovum from one, identified, living, adult woman'.[85] The use of IVD gametes would seem to violate this right, but it is not clear whether the community endorses this view.

Article 11 of the United Nations' *Universal Declaration on the Human Genome and Human Rights* states 'Practices which are contrary to human dignity, such as reproductive cloning of human beings, should never be permitted.' It continues by inviting 'states and competent international organisations' to 'cooperate in identifying such practices and in taking, at national or international level, the measures necessary to forbid them'.

[85] Somerville M. *Children's Human Rights to Natural Biological Origins and Family Structure.* Proceedings of the Jurisprudence of the Family: Foundations and Principles Symposium, May 28-29, 2010, Bratislava School of Law, Bratislava, Slovakia.

Both the Australian and the international community must therefore consider whether the use of IVD gametes for human reproduction is contrary to human dignity. To put this another way, the community must consider whether the use of IVD gametes in human reproduction is more like reproductive cloning (which is contrary to human dignity) or more like IVF (which might cause disquiet at first but which may come to be accepted by the majority of the community).

If Australia permits this technology for heterosexual couples, the community must also consider whether it would be either ethical or legal to deny the same technology to same-sex couples or single individuals.

The Review Committee encourages community discussion and debate to establish community standards about all these matters.

The Review Committee recommends that the reproductive use of human IVD gametes should not be permitted at the present time. It also recommends that research using human IVD gametes should be permitted under licence.

This recommendation should not be read as implying that the Review Committee thinks that the reproductive use of human IVD gametes should ultimately be permitted. Instead, it simply seeks an increase of scientific knowledge about human IVD gametes.

> **Recommendation 11:** (by majority) Section 20(1) of the *Research Involving Human Embryos Act 2002* should be amended to include that a person may apply to the NHMRC Licensing Committee for a licence authorising the creation and use of human embryos by fertilisation of a human egg by a human IVD sperm, fertilisation of a human IVD egg by human sperm, and fertilisation of a human IVD egg with human IVD sperm, in each case provided that the sperm and egg are not derived from the same person.

Reverend Kevin McGovern did not endorse Recommendation 11

> He was concerned that the development of knowledge about human IVD gametes will lead almost inevitably to their use in human reproduction, even if many in our society are opposed to this.

5.9.1 Definition of 'IVD Gametes'

NHMRC suggests the legislation should include a definition of *in vitro* derived (IVD) gametes (eggs and sperm) in order to properly differentiate naturally derived gametes.

The Review Committee agrees.

> **Recommendation 12:** The legislation should be amended to include a definition of IVD gametes. Such a definition could be 'human sperm or eggs derived from precursor cells or by *in vitro* means'.

5.9.2 Definition of 'Prohibited Embryo'

NHMRC suggests that for the purposes of s 20(4) of the *Prohibition of Human Cloning for Reproduction Act 2002* embryos created with the use of IVD sperm or eggs be included in the definition of 'prohibited embryo'.

The Review Committee agrees.

> **Recommendation 13:** Section 20(4) of the *Prohibition of Human Cloning for Reproduction Act 2002* should be amended to include embryos created with the use of IVD sperm or eggs in the definition of 'prohibited embryo'. Such a definition could include 'hybrid embryos within the meaning of s 8 of this Act'.

5.9.3 Definition of 'Hybrid Embryos'

NHMRC suggests that the definition of 'hybrid embryos' in s 8 of the *Prohibition of Human Cloning for Reproduction Act 2002 and s 7 of the Research Involving Human Embryos Act 2002* include the creation of hybrid embryos using IVD gametes.

The Review Committee agrees.

> **Recommendation 14:** The *Prohibition of Human Cloning for Reproduction Act 2002* should be amended to extend the definition of 'hybrid embryos' to include an embryo created by the use of IVD gametes. Such a definition could be 'In the foregoing human egg or human sperm includes IVD gametes'.

5.9.4 Commercial trade in IVD Gametes

NHMRC suggests that s 21 of the *Prohibition of Human Cloning for Reproduction Act 2002* be amended to make clear that the prohibition on commercial trade in human gametes extends to IVD gametes.

The Review Committee agrees.

> **Recommendation 15:** Section 21 of the *Prohibition of Human Cloning for Reproduction Act 2002* should be amended to include IVD gametes.

5.10 Definition of 'Human Sperm' and 'Human Eggs'

NHMRC suggests the legislation should include a definition of human sperm and human eggs. The Review Committee considers that once IVD gametes are defined, to specify them as an exceptional kind of sperm and eggs there is no need for a definition of the obvious type of eggs and sperm in this context, which is human sperm and eggs.

> **Recommendation 16:** There should be no specific definition of human sperm and egg.

5.11 Definition of 'Fertilisation'

NHMRC suggests there be a definition of fertilisation in s 8 of the *Prohibition of Human Cloning for Reproduction Act 2002.*

The Review Committee agrees.

> **Recommendation 17:** The *Prohibition of Human Cloning for Reproduction Act 2002* should be amended to include a definition of fertilisation.

5.12 Definition of 'Responsible Person'

NHMRC suggests definitions in s 8 of the *Research Involving Human Embryos Act 2002* for 'responsible person' clarify who is required to give consent in relation to donation of fetal tissues and who is required to give consent in relation to donation of failed-to-fertilise or abnormally fertilised eggs.

The Review Committee agrees.

The Review Committee noted that Chapter 4.1 of the *National Statement on Ethical Conduct in Human Research* permits the mother of a deceased fetus *ex utero* (along with anyone else whom she wishes to involve) to give consent for the use of tissue from that fetus in research. Further the Review Committee notes that failed-to-fertilise or abnormally fertilised eggs may contain DNA from sperm.

> **Recommendation 18:** Section 8 of the *Research Involving Human Embryos Act 2002* should be amended to clarify who is required to give consent in relation to donation of fetal tissues and who is required to give consent in relation to donation of failed-to-fertilise or abnormally fertilised eggs.

5.13 Licence Conditions as to the Number of Embryos or Eggs for which Consent can be Obtained

Section 24 of the *Research Involving Human Embryos Act 2002* deals with the conditions to which a licence may be subject by the Licensing Committee. One of the conditions specifically provided for, in s 24(5)(b), specifies the number of embryos or eggs to be *used* under the licence. However, there is no specific provision for limiting the number of embryos or eggs for which *consent* may be given.

Thus there is no specific power (other than under the general power in sub-s (4)) to impose a condition that ensures that consents are not obtained for a number of embryos or eggs far in excess of the number reasonably expected to be required.

NHMRC suggests such a specific condition be provided for. The Review Committee agrees.

> **Recommendation 19:** Section 24(5) of the *Research Involving Human Embryos Act 2002* should be amended to provide that a condition of a licence may include a limitation on the number of embryos or eggs for which consent is to be obtained prior to research use.

5.14 Limits on Storage of Excess ART Embryos

Section 8.8 of the NHMRC *Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research* (ART Guidelines) states that 'it is not desirable to leave embryos in storage indefinitely. Section 8.8.1 adds that 'the maximum time for which embryos may be kept in storage should be five years with the option to renew the consent for a further five years.' After this point, embryos must be used, donated for use in research, or arrangements must be made for respectful disposal of these embryos.

In its submission, NHMRC noted that concern had been expressed by the Licensing Committee that:

> some clinics might be storing excess embryos even though there is no research project, or indeed any prospect of a research project, available to use them – a situation which the Licensing Committee rightly describes as 'ethically undesirable'.

The Review Committee shares this concern and recommends that when excess embryos are donated for research, the maximum period for which those embryos may be kept in storage should be five years. If those embryos have not been used in research in that time, their custodians should arrange for the respectful disposal of those embryos.

The Review Committee further recommends that even within this five year period, if it becomes clear that those embryos are most unlikely to be used in research, clinics should again arrange for the respectful disposal of those embryos.

These recommendations should be considered when the current ART Guidelines undergo review.

> **Recommendation 20:** When the current NHMRC *Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research* undergo review, consideration should be given to including guidance that excess embryos donated for research should be kept in storage for a maximum of five years, after which their custodians should arrange for the respectful disposal of these embryos. Consideration should also be given to guidance that respectful disposal of these embryos should occur if it becomes clear even within that five year period that these embryos are most unlikely to be used in research.

5.15 Definition of 'Significant Advances'

Section 21(4) of the *Research Involving Human Embryos Act 2002* elevantly provides:

> (4) In deciding whether to issue the license, the NHMRC Licensing Committee must have regard to the following:
>
> (a) …
>
> (b) the likelihood of significant advance in knowledge or improvement in technologies for treatment as a result of the use of excess ART embryos or human eggs, or the creation or use of other embryos, proposed in the application, which could not reasonably be achieved by other means;
>
> (c) any relevant guidelines, or relevant parts of guidelines, issued by the CEO of the NHMRC under the *National Health and Medical Research Council Act 1992* and prescribed by the regulations for the purposes of this paragraph;
>
> (d) …
>
> (e) such additional matters (if any) as are prescribed by the regulations.

NHMRC suggests including criteria for assessing 'significant advance in knowledge or improvement in technologies for treatment' in the legislation or guidelines.

However, The Review Committee considers any such amendment would add unnecessary complication to the legislation.

The ordinary meaning of 'significant' in this context is 'important, notable' (Shorter Oxford English Dictionary), 'important, of consequence' (Macquarie Dictionary).

The Review Committee notes that the Licensing Committee has to consider not only the significance of the proposed advance, in the light of present common general knowledge amongst experts in the field, but the likelihood of that advance being achieved. Presumably the less significant the proposed advance, the greater would be the degree of likelihood required.

The expert members of the Licensing Committee will be able to apply the statutory standard to any proposed research. The Review Committee does not think the introduction of a series of boxes to be ticked would assist this evaluative process.

No specific examples of suggested criteria were submitted. To the extent that criteria were merely synonyms of the terms presently in the Act, they would be unhelpful. The legislation has to be applied in the future to projects in the light of the state of scientific knowledge at the time. The general standard of significant advance, to be applied in infinitely variable situations, is not susceptible to prescriptive definition. As the High Court said in discussing the term 'public interest' in freedom of information legislation:

> The terminology of the sub-section does not define a rule so much as an evaluative standard requiring restraint in the exercise of the power. It is, like many common law standards, predicated on fact-value complexes, not on mere facts' to be applied by the decision-maker.[86]

Recommendation 21: The term 'significant advance' in s 21(4) of the *Research Involving Human Embryos Act 2002* should not be the subject of legislative definition.

5.16 Direction to Withdraw Application

Section 21(2) of the *Research Involving Human Embryos Act 2002* provides that the Licensing Committee must decide whether or not to issue the licence sought.

NHMRC suggests that the Licensing Committee should have a third option, *viz* to require that an application be withdrawn if the Licensing Committee does not have sufficient information to allow it to make a decision to issue or not issue a licence.

The Review Committee agrees.

[86] *Osland v Secretary to the Department of Justice* [2010] HCA 24 at [14]

Recommendation 22: Section 21(2) of the *Research Involving Human Embryos Act 2002* should be amended to provide that the Licensing Committee may require that an application be withdrawn if the Licensing Committee does not have sufficient information to allow it to make a decision to issue or not issue a licence.

5.17 Revocation of Licence where Endpoints Achieved or Significant Advance not Expected

NHMRC suggests that the Licensing Committee should have power to revoke a licence if it considers that the endpoints of the project have been achieved or that the licensed activity no longer would be expected to lead to a significant advance.

The Review Committee agrees. However, the legislation should require that such revocation be only after notice has been given to the licence holder and the latter has had an opportunity to respond. Also there should be provision for suspension as well as revocation. Provision is made for suspension or revocation in s 26 of the *Research Involving Human Embryos Act 2002*. That section should be amended to provide for suspension or revocation on the grounds that the endpoints of the project have been achieved or that the licensed activity no longer would be expected to lead to a significant advance.

> **Recommendation 23:** Section 26 of the *Research Involving Human Embryos Act 2002* should be amended to provide that the Licensing Committee may, by notice in writing to the licence holder, suspend or revoke a licence if it considers that the endpoints of the licensed activity have been achieved or that the licensed activity no longer would be expected to lead to a significant advance.

5.18 Revocation of Licence on Reasonable Grounds

NHMRC suggests that s 26(1) of the *Research Involving Human Embryos Act 2002* be amended to provide that the Licensing Committee may suspend or revoke a licence if it believes on reasonable grounds it is necessary or desirable to do so. This would be in addition to the grounds discussed in 5.17.

The Review Committee agrees. This is a substantial extension of the Licensing Committee's powers. It should only be exercisable after written notice to the licence holder and the latter having had an opportunity to respond. Such a revocation (as with revocation or suspension on other grounds) would be subject to merits review by the Administrative Appeals Tribunal.

Recommendation 24: Section 26 of the *Research Involving Human Embryos Act 2002* should be amended to provide that the Licensing Committee may, by notice in writing to the licence holder, suspend or revoke a licence if the Licensing Committee believes on reasonable grounds it is necessary or desirable to do so.

5.19 Surrender of Licence with Consent

Section 27 of the *Research Involving Human Embryos Act 2002* provides that a licence holder may surrender a licence by giving written notice to the Licensing Committee.

NHMRC suggests that surrender should only be available with the prior consent of the Licensing Committee.

The Review Committee agrees. It is conceivable that the Licensing Committee may wish to investigate matters such as breach of licence conditions. The licence holder should not be able to thwart such an investigation by surrender of the licence.

Recommendation 25: Section 27 of the *Research Involving Human Embryos Act 2002* should be amended to provide that a licence may only be surrendered with the prior consent of the Licensing Committee.

5.20 Assessment and Approval by Human Research Ethics Committee

One of the essential requirements for the issue of a licence is that the activity or project has been assessed and approved by an HREC – *Research Involving Human Embryos Act 2002*, s 21(3)(c).

To remove any doubt, that Act should be amended, as NHMRC suggests, to provide that the HREC should have regard, amongst other things, to the matters which the Licensing Committee itself must have regard under s 21(3) and (4).

Recommendation 26: Section 21(3)(c) of the *Research Involving Human Embryos Act 2002* should be amended to provide that a HREC should have regard, amongst other things, to the matters which the Licensing Committee itself must have regard under s 21(3) and s 21 (4).

5.21 Membership of NHMRC Embryo Research Licensing Committee

The membership of the Licensing Committee, as provided for in s 16(1) of the *Research Involving Human Embryos Act 2002*, is as follows:

(a) a member of AHEC;

(b) a person with expertise in research ethics;

(c) a person with expertise in a relevant area of research;

(d) a person with expertise in assisted reproductive technology;

(e) a person with expertise in a relevant area of law;

(f) a person with expertise in consumer health issues relating to disability and disease;

(g) a person with expertise in consumer issues relating to assisted reproductive technology;

(h) a person with expertise in the regulation of assisted reproductive technology;

(i) a person with expertise in embryology

AHEC means the Australian Health Ethics Committee established by the National *Health and Medical Research Council Act 1992* as described in s8 of the *Research Involving Human Embryos Act 2002.* The Review Committee considers that the term consumer in s 16(1)(f) and s 16(1)(g) is intended to mean patient.

NHMRC suggests that the Licensing Committee should include a person with expertise in counselling issues relating to ART and a person with expertise in research and clinical applications of stem cells.

Presumably the suggested additions would be in addition to the nine existing members. In terms of administrative efficiency (amongst other things, all States and Territories have to be consulted on all appointments), not to mention expense, the Review Committee thinks that nine members for highly technical work of this nature are more than enough.

It seems highly unlikely that the Minister, in selecting a person with expertise in a relevant area of research (s 16 (1)(c)), would not select someone with stem cell expertise.

The Review Committee notes that, as to counselling issues, it is not the Licensing Committee that does the counselling. The Review Committee considers that if in any particular case the Licensing Committee thinks that it needs some extra assistance, there is nothing to stop it consulting such advisors that may have relevant expertise.

> **Recommendation 27:** There should be no change to the categories of membership of the Licensing Committee.

5.22 Hybrid Embryos: Note to s 23B(3) of the *Prohibition of Human Cloning for Reproduction Act 2002*

Section 20(1)(f) of the *Research Involving Human Embryos Act 2002* states that a person may apply for a licence for the creation of hybrid embryos by the fertilisation of an animal egg by a human sperm and the use of such embryos up to first mitotic division for the purpose of testing sperm quality. Section 21 empowers the Licensing Committee to issue such a licence.

Section 23B(1) and (2) of the *Prohibition of Human Cloning for Reproduction Act 2002* make it a criminal offence to create (subs (1)) or develop (subs (2)) a hybrid embryo . However subs (3) provides that the creation or development of a hybrid embryo is not an offence if it is authorised by a licence.

A Note to s 23B states:

> Note: A licence to create or develop a hybrid embryo can only be issued under section 21 of the *Research Involving Human Embryos Act 2002*:
>
> (a) for the purposes of testing sperm quality in an accredited ART centre – up to, but not including, the first mitotic division; or
>
> (b) in the case of hybrid embryo created by introducing the nucleus of a human cell into an animal egg – for not longer than 14 days.

Note (b) does not accurately state the effect of the *Research Involving Human Embryos Act 2002*. The latter Act only authorises licences for fertilisation of animal egg by human *sperm*. Note (b) refers to the introduction of the nucleus of a human cell into an animal egg. It is not lawful to issue a licence to do the research envisaged in Note (b). Although the Lockhart Committee recommended that the creation of such hybrid embryos under licence should be permitted, that recommendation was not accepted by the Parliament. The inclusion of this note was therefore an error in the amending process.

> **Recommendation 28:** Note (b) to s 23B(3) of the *Prohibition of Human Cloning for Reproduction Act 2002* should be amended to reflect s 20(1)(f) of the *Research Involving Human Embryos Act 2002*.

5.23 Reference to *Prohibition of Human Cloning for Reproduction Act 2002*

Sections 26(2) and 41 of the *Research Involving Human Embryos Act 2002* refers to the *Prohibition of Human Cloning Act 2002* (as it was originally legislated), instead of the *Prohibition of Human Cloning for Reproduction Act 2002*.

> **Recommendation 29:** Sections 26(2) and 41 of *Research Involving Human Embryos Act 2002* should be amended to refer to the *Prohibition of Human Cloning for Reproduction Act 2002*.

5.24 Reference to Assisted Reproductive Technology Guidelines and the National Statement

The *Research Involving Human Embryos Act 2002* and the *Prohibition of Human Cloning for Reproduction Act 2002* refer to the *Ethical guidelines on the use of assisted reproductive technology in clinical practice and research 2007 (ART Guidelines)* and the *National statement on ethical conduct in research involving humans 1999 (National Statement).*

The ART Guidelines and the National Statement are revised from time to time and when this occurs, the *Research Involving Human Embryos Act 2002* and the *Prohibition of Human Cloning for Reproduction Act 2002* will refer to outdated versions of these documents.

> **Recommendation 30:** The *Research Involving Human Embryos Act 2002* and the *Prohibition of Human Cloning for Reproduction Act 2002* should be amended to make reference to the *Ethical guidelines on the use of assisted reproductive technology in clinical practice and research* and the *National statement on ethical conduct in human research* as in force from time to time.

5.25 National Stem Cell Centre / National Stem Cell Bank

The *Research Involving Human Embryos Act 2002* and the *Prohibition of Human Cloning for Reproduction Act 2002* currently refer to a National Stem Cell Centre. The reference should be to a National Stem Cell Bank, as reflected in the Explanatory Memorandum for the 2006 amendments.

> **Recommendation 31:** The *Research Involving Human Embryos Act 2002* and the *Prohibition of Human Cloning for Reproduction Act 2002* should be amended to make reference to a National Stem Cell Bank instead of a National Stem Cell Centre

5.26 Prescribed Bodies which should be Consulted

Schedule 1 of the *Research Involving Human Embryos Act 2002* lists the prescribed bodies which should be consulted by the Minister for certain activities prescribed by the Act. Some of these prescribed bodies have changed status since the legislation was introduced, such as:

- the Australasian Biotechnology Advisory Council was part of Biotechnology Australia (BA). BA ceased operations on 30 June 2008, and consequently the Australasian Biotechnology Advisory Council no longer exists;
- the Australian Consumers' Association is now known as CHOICE;
- the Australian Vice-Chancellors' Committee is now known as Universities Australia;

- the Australian Institute for Health, Law and Ethics Inc became the Australian and New Zealand Institute for Health, Law and Ethics Inc and has now merged with the Australasian Bioethics Association Inc to become the Australasian Association of Bioethics and Health Law; and
- the Australian and New Zealand Infertility Counsellor's Association has joined the Fertility Society of Australia.

Recommendation 32: Schedule 1 of the *Research Involving Human Embryos Act 2002* should be updated to list the following prescribed bodies:

- The Australian Academy of Science
- ACCESS Australia's National Infertility Network Ltd
- CHOICE
- The Australian Research Council
- Universities Australia
- Consumers Health Forum of Australia
- The Law Council of Australia
- The Australian Federation of Disability Organisations
- The Royal College of Nursing, Australia
- The Australasian Association of Bioethics and Health Law
- The Australian Society for Medical Research
- The Fertility Society of Australia
- The Royal Australasian College of Physicians
- The Royal Australian and New Zealand College of Obstetricians and Gynaecologists
- The Royal Australian College of General Practitioners
- The Society for Reproductive Biology

5.27 Further Review of the Acts

Section 25A of the *Prohibition of Human Cloning for Reproduction Act 2002* and section 47A of the *Research Involving Human Embryos Act 2002* contain legislative provisions for review. The Acts state:

> The Minister must cause an independent review of the operation of this Act as amended by the *Prohibition of Human Cloning for Reproduction and the Regulation of Human Embryo Research Amendment Acts 2006* (the ***amending Act***) to be undertaken as soon as possible after the third anniversary of the day on which the amending Act received the Royal Assent.

Without amendment that provision would probably not operate to mandate a review after the present one; it only refers to one review, which is to occur after the third anniversary of the Royal assent to the amending Act, ie the 2006 Act.

The Review Committee thinks it highly desirable that in this rapidly changing field of science there be periodic reviews. For example, it may be that by the time of the next review it has become accepted that SCNT is no longer appropriate.

However the period of three years may be too short. The Review Committee suggests five years as a suitable review period.

> **Recommendation 33:** The *Research Involving Human Embryos Act 2002* and the *Prohibition of Human Cloning for Reproduction Act 2002* should be amended to provide for a review of these Acts be undertaken at five year intervals.

GLOSSARY

Adult stem cell (nonembryonic stem cell) (AS cell)	Stem cells found among the specialised cells of a tissue (such as liver, kidney or brain). Adult stem cells can renew themselves and generate cells to repair the tissue where they are found. They can also generate a range of other cell types.
Assisted reproductive technology (ART)	The application of laboratory or clinical techniques to gametes or embryos for the purposes of reproduction.
Blastocyst	A five- to seven-day-old human embryo produced by cleavage of a fertilised egg and consisting of a hollow ball of approximately 100–150 cells. It is made up of an outer layer of cells (the trophectoderm), a fluidfilled cavity (the blastocoel), and a cluster of cells on the interior (the inner cell mass). The blastocyst follows the morula and precedes gastrulation and appearance of primitive streak in the development sequence.
Cell division	Method by which a single cell divides to create two cells. This continuous process allows a population of cells to increase in number or maintain its number. See also Mitotic division.
Chromosome	Structure found in a cell nucleus that contains genetic information in the form of chromatin.
Clinical trial	A test of a new treatment or procedure in humans. Phase 1 trials involve a small number of participants and are concerned with safety. Phase 2 and 3 trials involve larger numbers of participants and test the effectiveness of the treatment.
Clone	A term used to describe one of a group of identical genes, cells or organisms derived from a single ancestor.

Cloning	The process of producing a clone. In terms of animals or humans, this involves creating and developing to birth an embryo formed by stimulating a single adult cell to develop without fertilisation.
Cloning to generate embryonic stem cells	The process of creating an embryo using cloning technology (usually somatic cell nuclear transfer) to generate embryonic stem cells that are matched to the person that donated the somatic cell. Also commonly called, 'therapeutic cloning', 'adult cell reprogramming', and 'nuclear transfer'.
Culture	The solution in which cells are grown for experimental research. Culture contains nutrients to feed the cells, as well as other growth factors that may be added to direct desired changes in the cells.
Cybrid Embryo	an embryo formed by transferring the nucleus of a human cell into an enucleated animal oocyte (egg). Note that cybrids are sometimes referred to as chimera, hybrid, interspecies embryo, and admixed embryo.
Cytoplasm	The contents of a cell (apart from the nucleus) formed from a complex protein matrix, in which the cell's contents are suspended.
Differentiation	The process whereby an unspecialised cell acquires the features of a specialised cell, such as a heart, liver, or muscle cell.
Deoxyribonucleic acid (DNA)	A chemical found primarily in the nucleus of cells and that is a major component of chromosomes. DNA carries the instructions for making all the structures and materials the body needs to function.
Embryo	The early developmental stage after fertilisation (see human embryo).

Embryonic stem cell (ES cell)	A cultured cell derived from the inner cell mass of a blastocyst. An embryonic stem cell can divide indefinitely and serve as a continuous source of new cells; under specific conditions, they can also differentiate into most other types of cells.
Embryonic stem cell line	Embryonic stem cells that have been cultured in the laboratory under conditions that allow cell division without differentiation for months to years.
Fertilisation	The process whereby male and female gametes unite.
Fetus	A developing human from two months after conception to birth.
Gamete	A human sperm or egg cell.
Gene	A functional unit of heredity that is composed of DNA and located in a specific site on a chromosome. A gene directs the formation of an enzyme or protein.
Genome	The complete genetic material of an organism.
Human embryo	A live embryo that has a human genome or an altered human genome and has been developing for less than eight weeks since the appearance of two pro-nuclei or the initiation of its development by other means.
Implantation	The process when the blastocyst embeds into the endometrium (lining of the uterus) to form a pregnancy.
Induced pluripotent stem (iPS) cells	A type of pluripotent stem cell artificially derived from a non-pluripotent cell, typically an adult somatic cell, by inducing a "forced" expression of certain genes.
Intracytoplasmic sperm injection (ICSI)	An assisted reproductive technology technique where a sperm is injected into an egg to assist fertilisation.

In vitro	Literally means 'in glass'; in a laboratory dish or test tube; an artificial environment.
In vitro derived (IVD) gametes	Recent research into IVD gametes has shown that gametes (sperm and eggs) can be derived from other types of cells. These cells include stem cells, precursor cells from fetal tissue, and cells produced by experimentally halving the number of chromosomes in somatic cells (somatic cell haploidization).
In vitro fertilisation (IVF)	An assisted reproductive technology technique in which fertilisation is carried out in the laboratory.
Mesenchymal stem cells	Adult stem cells with the ability to generate cartilage, bone, muscle,tendon, ligament and fat.
Mitochondria	Structures in the cytoplasm that turn nutrients into energy for the cells.
Mitochondrial DNA	DNA found in the mitochondria. It is passed down from a mother to her children in the egg cytoplasm.
Mitotic division	Cell division where the diploid number of chromosomes is maintained.
Nucleus (plural nuclei)	The dense part at the centre of a cell containing the cell's genetic material.
Oocyte	An egg cell.
Oocyte activation	Process whereby an egg is activated to start embryonic development.
Preimplantation genetic diagnosis (PGD)	A procedure used to test embryos for genetic abnormalities before placing them into a woman to establish a pregnancy.
Pluripotent	Ability of a single stem cell to develop into many different cell types of the body, including cell types from all three germ layers.

Precursor cell	A cell that is the parent cell of a specialised cell. Progenitor and precursor cells are different from stem cells because they cannot regenerate themselves.
Regenerative medicine	Treatments in which cells are transplanted into specific sites in the body to repair damaged or deficient cell populations or tissues.
Reproductive cloning	Using cloning technology (usually somatic cell nuclear transfer) to create an embryo that is implanted into a woman for gestation and birth.
Somatic cell	One of the cells that take part in the formation of the body, becoming differentiated into the various tissues, organs, etc. This cell can form any cell in the body except a germ cell (including gametes).
Somatic cell nuclear transfer	Moving the nucleus and its genetic material from a somatic cell to another cell (usually an egg cell from which the genetic material has been removed).
Stem cells	Cells that have the capacity to both self-renew and differentiate into a variety of more mature and specialised cells through the process of cellular differentiation.
Therapeutic cloning	Term previously used to describe cloning to generate embryonic stem cells.

ABBREVIATIONS

ART	Assisted Reproductive Technology
ASCC	Australian Stem Cell Centre
DNA	Deoxyribonucleic acid
ES cell	Embryonic stem cell
GIFT	Gamete intrafallopian transfer
HREC	Human Research Ethics Committee
ICSI	Intracytoplasmic sperm injection
iPS cells	Induced pluripotent stem cells
IVD gametes	In vitro derived (IVD) gametes
IVF	In vitro fertilisation
NHMRC	National Health and Medical Research Council
PGD	Preimplantation genetic diagnosis
SCNT	Somatic Cell Nuclear Transfer

See the Glossary definitions of terms used

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113	149	Reverend. Ramon Robinson	Katoomba Anglican Church
114	150	Confidential	Private Submission
115	151	Mr Mark Smith	Anglican Church, Kirribilli
116	152	Mr Reuben Scott	Private Submission
117	153	Confidential	Private submission
118	154	Blair Courtney-O'Connor	Private submission
119	155	Mr Anton Marquez	Private submission
120	156	Confidential	Private submission
121	157	Mr Andrew Copp	Private
122	158	Mr Phil Case	Private submission
123	159	Mr Simon Kaufman	Private submission
125	161	Mr Paul Grimmond	Private submission
126	162	Mr Richard Maude	Private submission
127	163	Confidential	Private submission
124	164	Professor Martin Pera	University of Southern California
128	165	Confidential	Private submission
129	166	Ms Elizabeth Fong	Private submission

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130	167	Confidential	Beverly Hills Anglican Church
131	168	Ms Jane Lister	Private submission
132	169	Mr Clive Ellis	Private submission
133	170	Confidential	Private submission
134	171	Mr Nathan Lowery	Private submission
135	172	Confidential	Private submission
136	173	Confidential	Private submission
137	174	Mr Anthony King	Private submission
138	175	Dr Peter Barnes	Evangelicals for Life
139	176	Confidential	Northern Lakes Evangelical Church
140	177	Reverend Michael Paget	St Barnabas Anglican Church, Broadway
141	178	Confidential	Private submission
142	179	Ms Emma Thornett	Private submission
143	180	Ms Joanna Knott	Spinalcure Australia
144	181	Mr Stephen Watt	Private submission
145	182	Ian Millican	St Mark's Anglican Church, Berowra
146	183	Reverend Diane Harvey	Private submission
147	184	Confidential	Douglas Park Evangelical Church
148	185	Ms Emma Lovegrove	Private submission
149	186	Ms Lynette Johnston	The Australian Family Association
150	187	Mr Michael Blake	Private submission
151	188	Ms Janet Sietsma	Private submission
152	189	James and Tracey Nodder	Private submission
153	190	Confidential	Private submission
154	191	Ms Jennifer Roach	Private submission
155	192	Dr Robert Pollnitz	Paediatrics SA

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156	193	Confidential	UK Stem Cell Bank NIBSC-HPA
157	194	Mr Craig Stevens	Private submission
158	195	Confidential	Private Submission
159	196	Anne-Maree, Margaret, Margaret-Mary and Anthony Althaus	Private submission
160	197	Ms Katie McFarlane	Private submission
161	198	Confidential	Private submission
162	199	Confidential	Private submission
163	200	Mr Martin Shadwick	Snowflakes Australia
164	201	Confidential	Private submission
165	202	Confidential	Private submission
166	203	Mr Gerard Calilhanna	Private submission
167	204	Mr Christopher Braga	Summer Hill Church
168	205	Mr Thomas Ong	Credo – AFES group at UTS
169	206	Confidential	Private submission
170	207	Mr David Piper	Lightning Ridge Community Church (Anglican Diocese of Armidale)
171	208	Confidential	Private submission
172	209	Mr Michael Casanova	Private submission
173	210	Confidential	Private submission
174	211	Ms Carol Birks	MND Australia
175	212	Professor Alan Trounson	California Institute for Regenerative Medicine
176	213	Confidential	Private submission
177	214	Confidential	Private submission
178	215	Confidential	Private submission
179	216	Confidential	Anglican Church Diocese of Sydney
180	217	Dr Andrew Pesce	Australian Medical Association
181	218	Mr Akos Balogh	Private submission

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182	219	Confidential	Private submission
183	220	Confidential	Private submission
184	221	Ms Melinda Tankard Reist	Private submission
185	222	Mr David Phillips	FamilyVoice Australia
186	223	Mr John Miller	Private submission
187	224	Confidential	Private submission
188	225	Confidential	Private submission
189	226	Mr Paul Russell	New South Wales Right to Life
190	227	Ms Sara Fraser	Private submission
191	228	Mr Roger McWhinney	Private submission
192	229	Albert and Carol Phillips	Private submission
193	230	Confidential	Private submission
194	231	Dr Megan Munsie	Australian Stem Cell Centre
195	232	Mr Rory Killen	Australian Sex Party
196	233	Mr David Yu	Private submission
197	234	Confidential	Private submission
198	236	Confidential	Private submission
199	237	Mr Alan Baker	Family Council of Queensland
200	238	Ms Varlli Beetham	Friedreich Ataxia Research Association (Australasia)
201	239	Mr Peter McTackett	Private submission
202	240	Dr David van Gend	National Director, Australians for Ethical Stem Cell Research
203	241	Dr Megan Best	Social Issues Executive Sydney Diocese Anglican
204	242	Mr Harry Pobjoy	Private submission
205	243	Dr Julia Schaft	Sydney IVF Limited
206	244	Mr Jerome Appleby	Australian Family Association (SA Branch)
207	245	Confidential	Private submission

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208	246	Mr Duncan Andrews	Private submission
209	247	Mr Ben Williams	Australian Christian Lobby
210	248	Mr Dennis Clarke	Private submission
211	249	Confidential	Private submission
212	250	Confidential	Private submission
213	251	Jennifer and Shann Kellaway	Private submission
214	252	Dr Donna Purcell and Ms Teresa Martin	Cherish Life Queensland Inc
215	253	Dr Susan Hawes	Australasian Society for Stem Cell Research
216	254	Mr Peter McArdle	Australian Catholic Bishops Conference
217	255	Mr Jeremy Wright	MS Australia
218	256	Ms Varlli Beetham	CAMRA – Coalition for the Advancement of Medical Research Australia
219	257	Dr Stephanie Williams	The Spinal Cord Injury Network
220	258	Professor Justin St. John	Monash Institute of Medical Research
221	259	Ms Jenny Stokes	Salt Shakers
222	260	Mr Tim Patrick	Private submission
223	261	Professor Richard Boyd	Monash University
224	262	Mr Paul Groves	Private submission
225	263	Confidential	Private submission
226	264	Ms Polly Seidler	Private submission
227	265	Mr Marc Peschanski	Stem Pole network
228	266	Mr Matthew Murphy	Private submission
229	267	Reverend Les Percy	Minister of the Presbyterian Church of Australia
230	269	Mr Peter Murray	Private submission
231	270	Simonette Foletti	Private submission

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232	271	Mr Jody Trouncer	Private submission
233	272	Confidential	Private submission
234	273	Mr Rob Elder	Private submission
235	274	Ms Jenny Jones	Private submission
236	275	Confidential	De La Salle Brothers Scarborough
237	276	Mr Tim Cannon	Australian Family Association
238	277	Confidential	Private submission
239	278	Mr Lewis Jones	Private submission
240	279	Mr RV and Mrs PJ Barbero	Private submission
241	280	Ms Sally Stark	Private submission
242	281	Dr Peter McCullagh	Private submission
243	282	Mr Marcia Riodan and Dr Denise Cooper-Clarke	Ad Hoc Interfaith Committee
244	283	Rabbi Shimon Cowen	Private submission
245	284	Confidential	Monash Institute of Medical Research
246	285	Confidential	FINRRAGE (Australia)
247	286	Associate Professor Peter Illingworth	Fertility Society of Australia
248	287	Confidential	Medicine with Morality
249	288	Confidential	Private Submission
250	289	Confidential	Private Submission
251	290	Confidential	Private Submission
252	291	Confidential	Regulatory Institutions Network, Australian Nation University
253	292	Confidential	Private Submission
254	293	Confidential	Private Submission
255	294	Confidential	Deputy Vice-Chancellor (Research University of Sydney
256	295	Confidential	Presbyterian Church of Australia
257	296	Confidential	Uniting Church of Australia

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258	297	Confidential	Department of Health, Western Australia
259	298	Mr Adam Johnston	Private submission
260	299	Mr Darren Atkinson	Department of Innovation, Industry, Science and Research
261	300	Professor Warwick Anderson	National Health and Medical Research Council
262	301	Ms Jennifer Bray	Private Submission
263	302	Ms Iris Robinson	Private Submission
264	303	Confidential	Private Submission

SCHEDULE 2

Appearances

1. Dr Peter McCullagh, John Curtin School of Medical Research
2. Professor Jock Findlay, Professor Don Chalmers, NHMRC Licensing Committee
3. Dr Gregory Pike, Southern Cross Bioethics Institute
4. Professor Robert Williamson, Dr Martin Callinan and Dr Fiona Leves, Australian Academy of Science
5. Dr Sandra Hacker, Dr Nikoljas Zeps, Australian Health Ethics Committee
6. Ms Varlli Beetham, Carrie Beetham, David Prast and Mary Webb, Coalition for the Advancement of Medical Research Australia
7. Dr Megan Munsie, Professor Joe Sambrook, and Professor Andrew Elefanty, Australian Stem Cell Centre
8. Ms Deb Andrews, Dr Nyaree Jacobsen, Adjunct Associate Professor Maureen Harris, Office of the Chief Medical Officer Western Australia
9. Dr David van Gend, Australians for Ethical Stem Cell Research
10. Dr Tomas Stojanov, Dr Kylie deBoer and Asha Robinson, Sydney IVF
11. Professor Alan Mackay-Sim, Griffith University
12. Ms Kerry Doyle, Department of Trade and Industry, Regional Infrastructure and Services and Julie Letts, Department of Health, New South Wales Government
13. Dr Phil Davies, Dr Ross Bury, Ms Anne Brown, Victorian Government
14. Rabbi Dr Shimon Cowen, Institute for Judaism and Civilization

Professor John Martin was invited to meet with the Review Committee. He was overseas at the time, and therefore unable to do so.