Legislation Review:
***Prohibition of Human Cloning Act 2002* and**
Research Involving Human Embryos Act 2002

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Legislation Review Committee

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Letter of transmittal

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

19 December 2005

The Hon Julie Bishop MP
Minister for Ageing
Parliament House
CANBERRA ACT 2600

Dear Minister

In accordance with section 25(3) of the *Prohibition of Human Cloning Act 2002* and section 47(3) of the *Research Involving Human Embryos Act 2002*, I am pleased to present the reports of the reviews of both Acts.

The reports represent the consensus view of the Legislation Review Committee.

In order to complete the Terms of Reference for the Committee the reports are referred for tabling in both Houses of Parliament and presentation to the Council of Australian Governments.

Yours sincerely

John S Lockhart AO QC
Chair
Legislation Review Committee

cc The Hon John Howard MP
Prime Minister

Foreword

The task before the Legislation Review Committee has been challenging. The issues of human cloning and research involving human embryos raise important questions of morality, social values, ethics, alleviation of human distress and scientific research. To mention some of them:

- When does human life begin?
- How far should society allow research involving human embryos?
- What safeguards should surround the research?
- Should human embryos be accorded the same rights as human beings after birth?
- How should 'human embryo' be defined?
- What safeguards should be provided to protect the rights of women?
- Can common ground be found between the widely varying, indeed divergent, views of morality held by members of our society?
- Should society declare activities to be illegal, with all the attendant consequences of criminal conduct, when there is a wide range of ethical views on those activities?
- What are the limits of the use of in vitro fertilisation (IVF) and related methods (collectively known as assisted reproductive technology, or ART) and human embryo research?
- Should excess ART embryos continue to be available for research, with permission under licence?
- Should the creation of human embryos for research purposes be permitted?
- Should the creation of human embryo clones by somatic cell nuclear transfer be permitted, under licence, for research, training and clinical applications?
- Should an Australian stem cell bank be established?

These are large questions. There are others. Since the Committee was established earlier this year, it has grappled with all of them in forming its views and reaching its conclusions.

The Committee's terms of reference required it to consider a large number of issues and to consult widely. The fact that all States and the Australian Capital Territory have enacted complementary legislation added to this necessity. Indeed, we visited all States and Territories (except Tasmania, where we conducted a video conference) gathering information, received over a thousand written submissions, and spoke directly to people holding widely divergent views.

In looking for common ground, the Committee found that there is strong community support for medical research to help people who suffer from debilitating or incurable disease or conditions, through better understanding of the processes of disease and the development of new treatments.

There is also considerable community support for medical research to help people to have children, including a general acceptance that this process involves the 'wastage' of some embryos.

For some people, the values attached to treating disease and overcoming infertility are more important than the value of an embryo. For others, the value of an embryo, as a potential human being, is predominant.

My colleagues on the Committee are Associate Professor Ian Kerridge, Associate Professor Pamela McCombe, Professor Barry Marshall, Professor Peter Schofield and Professor Loane Skene. They provided a wide range of skills and experience that proved invaluable in considering the issues in these reviews.

I thank my colleagues for their conspicuous dedication and tireless effort to the tasks before us. It has been a privilege for me to chair the Committee.

I also thank the people and groups that supported our reviews. Secretariat Australia provided overall secretariat support to the reviews. Biotext was responsible for assisting us in writing and producing these reports. McNiece Communications provided communication support and advice during the review. The Committee also received considerable administrative support from the National Health and Medical Research Council.

Finally, I wish to thank all individuals and groups who contributed to our reviews. The exchange of views by participants during our public hearings throughout Australia were sometimes lively, but generally conducted by all concerned with courtesy and concern or sympathy for the views of others who held different views.

We have considered all these views in arriving at our conclusions and have set out many of them in our two reports. It is now for the Australian Parliament and the Government to take this matter forward through the Council of Australian Governments (COAG) process. We will watch with interest. We offer our views and recommendations to the Australian Parliament and COAG.

John Lockhart
Chair
19 December 2005

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Executive summary

Background to the reviews

In the 1990s, developments in assisted reproductive technology (ART), including in vitro fertilisation (IVF) and other related methods, raised significant ethical issues about what forms of human reproduction may be possible or acceptable. At the same time, developments in other areas of biotechnology and medical research raised concerns about what uses of human embryos should be permitted for research purposes.

The *Prohibition of Human Cloning Act 2002* (PHC Act) and the *Research Involving Human Embryos Act 2002* (RIHE Act) were passed in 2002 to provide a national framework for regulation of these issues. The two Acts prohibit human cloning and several other reproductive practices; prohibit the creation of human embryos, by any means, other than to help a woman become pregnant; and allow the use for research, under strict regulation and licence, of human embryos created through ART but that are no longer needed by the couple for whom they were created.

Each Act required an independent review of its operation by 19 December 2005. In June 2005, the Hon Julie Bishop MP, Minister for Ageing (the minister with portfolio responsibility for human cloning and stem cell research), appointed the six–member Legislation Review Committee ('the Committee'). The Minister for Ageing and the Chief Executive Officer of the National Health and Medical Research Council (NHMRC) provided the Committee with terms of reference for the reviews of both Acts.

The Committee consulted the community extensively through a review website, written submissions, face-to-face meetings with key stakeholders, public hearings and some private meetings (at stakeholders' requests), facilitated stakeholder discussion forums, and selected site visits. In addition, the Committee reviewed the latest results of focus group and telephone survey research by the Public Awareness Program of Biotechnology Australia, and a literature review (commissioned by the NHMRC on behalf of the Minister for Ageing) of recent scientific and technological advances in human cloning, human embryo research and related matters, including stem cell technologies. Information from all these sources is summarised in this document, which forms the Committee's reports for the reviews of both Acts. This information contributed to the deliberations of the Committee and its considered view and led to 54 recommendations.

Rationale for the recommendations

Australian society is made up of diverse 'communities' with different perspectives, interests and values. Furthermore, an individual may be the member of multiple communities, each with divergent perspectives, or 'standards', and these standards vary between and within communities and over time. Because of these divergent values and interests represented within Australian society, the Committee has accepted that some disagreement will remain, whether or not any changes are made to the two Acts.

However, certain moral values are held in common by all communities, such as commitment to social justice and equity and to the care of vulnerable people. This is reflected in broad community support for medical research aimed at understanding, preventing or treating disease, and for research and clinical practice aimed at assisting people to have children (including a general acceptance that this process may involve the 'wastage' of some embryos). Therefore, in considering whether certain activities should be made illegal, the social and moral value that some communities attach to the human embryo needs to be balanced against the social and moral value that other communities attach to the treatment of disease and to helping people to have a family.

In framing the recommendations for these reviews, the Committee considered that the higher 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. In addition, even though some people think that an activity is unethical, it does not necessarily follow that that activity should be made illegal. Furthermore, the wider the range of ethical views on a particular activity, the weaker becomes the case for declaring that activity to be illegal, with all the attendant consequences of criminal conduct.

However, despite the divergent views received by the Committee during the reviews, both proponents and opponents of embryo research agreed that the current system of legislation is valuable. Therefore, the Committee recommended a continuation of national legislation imposing prohibitions on human reproductive cloning and some other ART practices, as well as strict control and monitoring, under licence, of human embryo research.

Prohibited practices

Overall, the Committee heard strong agreement between all groups that human reproductive cloning should continue to be prohibited on ethical grounds. The serious health and safety issues associated with the birth of live cloned animals also preclude consideration of this procedure in humans. The Committee has therefore recommended maintaining the prohibition of human reproductive cloning.

In terms of the other prohibited embryos mentioned in the PHC Act (embryos created by nuclear transfer or other methods not involving fertilisation of eggs by sperm, human–animal hybrid or chimeric embryos, embryos with genetic material from more than two persons, embryos with genetic alterations and so on), the strongest community objection was to the implantation of such prohibited embryos in a woman's body or to their development in any other way beyond 14 days. Therefore, the Committee has recommended that use of such embryos for reproductive purposes (that is, development beyond 14 days or implantation into a woman's reproductive tract) should remain prohibited.

The Committee has also recommended continuing the prohibition of placing any human embryo into an animal or into the body of a human apart from in a woman's reproductive tract, or placing an animal embryo into the body of a human for any period of gestation, because these practices are repugnant to the community. Similarly, the Committee did not hear any arguments for lifting the prohibition on the collection of viable embryos from a woman and therefore considers that this prohibition should continue.

Creating a human embryo by fertilisation of an egg by sperm

A range of views was expressed to the Committee on the status of human embryos, and their creation and use in research and to develop therapeutic products. Proponents of embryo research argued that the potential benefits of these activities meant that it would be unethical not to pursue the research and development made possible by such technologies. They also argued that current ART arrangements already sanction the possibility of the destruction of embryos, in the process of helping people to have a family, and hence not to allow embryo destruction to help people with other medical problems would be unfair. Opponents of embryo research argued that a human embryo, from the earliest stage of development, is an entity that deserves full protection and it is wrong to create such an entity for any purpose apart from ART treatment of a woman.

The Committee also learnt that different people and groups hold differing views about the meaning and use of the term 'embryo', both in medical science and as a more general term. The Committee considers that it is essential that the terminology used in the legislation is biologically accurate, clearly understandable by all stakeholders, and unambiguous to regulators, scientists and the public. However,

while it is critical to be clear about the terminology used, definitional clarity does not, in itself, resolve moral concerns and it is likely that, whatever language is used, different moral interpretations will be made regarding the status of such entities and the obligations owed to them.

Although a range of views was expressed about the precise moral status of preimplantation embryos in particular, there was an overall acceptance that human embryos created by the fertilisation of a human egg by a human sperm are entities of some social and ethical significance because of their association with the start of human life. Therefore, the Committee has recommended that the prohibition on the creation of an embryo by the fertilisation of a human egg by human sperm for any purpose apart from ART treatment of a woman should continue.

However, the Committee was concerned to hear that this provision, combined with the current definition of a human embryo as starting from the appearance of two pronuclei — a very early stage in fertilisation before the male and female genetic material combine — has had the apparently unintended consequence of impeding valuable research and clinical practice in ART clinics. In particular, the legislation has stopped research on culture and maturation of immature eggs (called 'in vitro maturation of oocytes', or IVM), storage of frozen eggs, various aspects of IVF, and gamete (egg and sperm) development. Research on maturation of eggs has been further prevented by the prohibition on oocyte activation (also called 'parthenogenesis'). The ability to produce mature eggs in culture provides a way of reducing the treatment of woman with follicle stimulating hormone, which would benefit many women undergoing ART. It may also allow production of mature eggs from frozen ovarian tissue, thus allowing women who have undergone chemotherapy or other treatments that reduce ovarian function to have their own genetic children.

Adopting an independently developed definition of a human embryo[1] to a slightly later stage in the fertilisation process (the first cell division) would allow much of the research described above to occur without falling outside the scope of the RIHE Act. This change would also maintain a very broad definition of an embryo, in line with all the community views expressed during the reviews, including that a new and unique genetic entity is formed only after the genetic material from the male and female pronuclei combine. This stage is known as 'syngamy' and occurs about one to three hours before the first cell division (cleavage).

However, fertilisation would only be allowed to progress up to, but not including, the first cell division. To achieve this change, the Committee has recommended that the definition of a human embryo created by fertilisation of a human egg by a human sperm should include the fertilised egg from the first mitotic cell division (cleavage). In addition, the current prohibition of the creation of hybrid embryos has prevented the use of a standard test for sperm maturity by experimental fertilisation of animal eggs. The Committee has therefore also recommended that hybrid fertilisation should be permitted, under licence, up to, but not including, the first cell division.

Use of excess ART embryos

Excess ART embryos have been used for research and other activities to improve the clinical practice of ART or for the derivation of embryonic stem cells. Overall, there was support for the use of excess ART embryos in research under the provisions of the RIHE Act. This view was also heard from ART consumers, many of whom have donated their excess embryos for research. The Committee has recommended that the use of excess ART embryos continue to be permitted, under licence, for research, training and other uses to improve the practice of ART.

1. NHMRC (2005). *Discussion Paper: Human Embryo — A Biological Definition*, NHMRC, Canberra. http://www.nhmrc.gov.au/embryos/index.htm (from January 2006)

Although some respondents suggested that ART clinics produce more ART embryos than required for treatment in order to ensure a supply of excess ART embryos, the Committee received no evidence that this is the case. Furthermore, ART clinics told the reviews that more excess ART embryos have been donated for research than there are research projects to use them. The Committee has therefore suggested that consideration should be given to a register of excess ART embryos available for research to facilitate the most efficient use of this resource.

The sunset clause in the RIHE Act (s46), which has now lapsed, was a response to similar concerns in 2002, and was an instrument of government to provide time for the development of an appropriate licensing and inspection system. The licensing system is now in place and the Reproductive Technology Accreditation Committee (RTAC) monitoring and annual reporting mechanisms for ART clinics are well established. Therefore, the Committee concluded that there is no further need to restrict the use of excess ART embryos to those produced before a specified date or for any further mechanism for monitoring of this process.

Information from the reviews showed that the status of embryos that are unsuitable for implantation is not clear in the current legislation. Such embryos are currently discarded, but researchers and ART practitioners indicated that these embryos would be useful for research, training and quality assurance activities. The Committee has therefore recommended that embryos that are not suitable for implantation should be permitted to be used for research, training and improvements in clinical practice and that the NHMRC should develop ethical guidelines for these uses. However, objective criteria should be developed by an expert body, against which decisions on declaring an embryo not suitable for implantation could be made. These criteria could include embryos that have not undergone mitotic divisions, carry additional pronuclei or show other major chromosomal defects, as well as those diagnosed by preimplantation genetic diagnosis (PGD) as having serious genetic defects.

In terms of using excess ART embryos to derive stem cells, research using excess ART embryos under licence since 2002 has yielded a number of new embryonic stem cell lines and researchers are working with these to further refine the methods of cell culture and differentiation that will be needed to develop cellular therapies. The Committee carefully considered all the submissions on embryonic stem cell research and equivalent research on adult stem cells and noted the following issues:

- many of the arguments made in favour of or against embryonic stem or adult stem cell research were speculative
- it is not possible, or helpful, to try to establish the relative experimental or potential therapeutic merits of embryonic stem and adult stem cells
- while embryonic stem cell research findings have not yet translated into any clinical trials or treatments, the use of excess ART embryos to derive embryonic stem cell lines has contributed to progress in the derivation and culture of the cells and in methods of promoting the growth of different cell types
- there have also been many preliminary findings in animal studies that indicate sufficient potential to warrant further investigation
- the range of diseases and conditions involved is substantial, and the number of people who may ultimately benefit from stem cell research is high.

These developments have continued to highlight moral and social questions about the use of human embryos in research. Indeed, it was clear to the Committee that much of the debate regarding the relative merits of embryonic and adult stem cell research was underpinned by differing attitudes towards the moral status of human embryos, and at times it was difficult to distinguish moral arguments from scientific or biological ones. This requires that all arguments be carefully examined not only in terms of the accuracy or lucidity of the argument itself, but also in terms of the values or

interests of the individual or group making the argument. Overall, the Committee therefore considered that further research on all aspects of stem cell biology, including those from embryonic and adult sources, is required to ensure that the potential of this field is fully realised.

Creation of embryos other than by fertilisation

The Committee also heard that further development of embryonic stem cell research requires creation of human embryo clones to generate embryonic stem cells that are either patient-matched for development of specific cellular therapies, or of known genotype for disease modelling and other research (so-called 'therapeutic cloning'). The Committee has reached an opinion, based especially on the evidence of experts who work directly in one or both fields (adult or embryonic) of stem cell research, that further research is required to improve knowledge and develop effective disease treatments. However, during the reviews, the Committee heard a number of objections to methods of creating human embryos not involving fertilisation of an egg by a sperm (including somatic cell nuclear transfer (SCNT)) to generate embryonic stem cells.

One argument was that the technology is the same as that used for reproductive cloning and therefore allowing cloning to extract stem cells would inevitably lead to the use of cloning technology for reproduction. However, as discussed above, the Committee has recommended that development of human embryos created by any method not involving fertilisation of an egg with sperm beyond 14 days, or implantation of such an embryo into a woman's reproductive tract, should continue to be prohibited to ensure that such embryos are not used for reproductive purposes.

A further argument was that it is wrong to create human embryos to destroy them and extract stem cells. Human embryo clones are human embryos and, given the right environment for development, could develop into a human being. Furthermore, if such an embryo were implanted in the uterus of woman to achieve a pregnancy, the individual so formed would certainly have the same status and rights as any other human being. However, a human embryo clone created to extract stem cells is not intended to be implanted, but is created as a cellular extension of the original subject. The Committee therefore agreed with the many respondents who thought that the moral significance of such a cloned embryo is linked more closely to its potential for research to develop treatments for serious medical conditions, than to its potential as a human life.

Furthermore, the production and destruction of such an embryo is not dissimilar to the production and destruction of excess ART embryos, which is permitted by the legislation and widely accepted by society. Thus, to permit one (production and destruction of ART embryos) but not the other (production and destruction of nuclear transfer and other bioengineered embryos) would be inconsistent and appear to attach more importance to the treatment of infertility than to the treatment of other diseases and conditions that could be helped as a result of this activity. In view of the wide range of diseases and conditions that stem cell research aims to help, and the burden of disease involved, the Committee has recommended that the creation of human embryo clones by SCNT should be permitted, under licence, for research, training and clinical applications.

In line with this recommendation, the Committee could also see potential benefits in other areas of research involving the creation of human embryos or human embryo clones by methods not involving fertilisation of a human egg by a human sperm. The Committee has therefore recommended that creation of such entities should also be permitted, under licence, for use in research, training and clinical applications. Similarly, creation of human embryos using the genetic material from more than two people, including heritable alterations to the genome or using precursor cells from a human embryo or fetus, should also all be permitted, under licence, for research to increase knowledge or treat diseases. The prohibition on developing a human embryo for more than 14 days and on implantation into the reproductive tract of a woman will prevent any of these embryos from being used for reproductive purposes.

Egg donation

A significant argument against the use of somatic cell nuclear transfer was that it requires the use of donated human eggs. The difficulties associated with attracting women to donate oocytes for research and with obtaining meaningful consent were seen as a major problem by many participants in the reviews. In this regard, the donation of eggs is riskier for the donor than the donation of other tissues, and the healthiest eggs would be those from young women. Therefore, the potential exists for coercion of young women to donate eggs (such as through social disadvantage, family or workplace pressures). Women in ART treatment programs may also be requested to donate eggs for research and, therefore, to avoid coercion of women in this situation, there needs to be clear separation between the obtaining of eggs for ART practice and research. While acknowledging that there is no completely satisfactory or generally agreed resolution to the issues raised by oocyte donation for research, the Committee has therefore recommended that egg donation should be managed by strict ethical guidelines (see below) and that payment to donors should not be permitted beyond reimbursement of reasonable expenses.

Furthermore, the Committee noted other sources of eggs, such as from frozen ovarian tissue or production of eggs from stem cells, may become available as research progresses and considered that use of these sources should be encouraged. In addition, the Committee has recommended that, to reduce the need for human eggs during the developmental stages of nuclear transfer research, use of animal oocytes should also be permitted, under licence (as long as all the requirements of the amended Acts in this regard are satisfied and that these embryos are not implanted into the body of a woman).

Licensing arrangements and oversight of ART services

Respondents to the reviews considered that the Licensing Committee fulfils a valuable role. The Committee has recommended that this role should be expanded to include licensing of the additional activities recommended in these reviews. However, the Committee supports the role of the institutional human research ethics committees (HRECs) and the dual system of approval, initially by the HREC, followed by application for a licence from the Licensing Committee. Therefore, although the Committee's recommendations allow a larger number of research proposals, institutional HRECs will be able to allow or decline specific research proposals for their institution.

During the reviews, the Committee heard that training and quality assurance activities at ART clinics have been impeded by the current licensing arrangements, which are not well suited to these activities. While all research involving human embryos should continue to require a licence, the Committee has recommended that the licensing process for training and quality assurance activities at ART clinics should be facilitated by the Licensing Committee developing a simplified proforma application for these activities.

Informed consent for embryo and egg donation was an important issue in the public consultation process. All stages of consent were seen as having an emotional component, with many people inclined to donate excess embryos to research rather than letting them succumb.

Donors of excess ART embryos expressed concerns that the current process for declaration of embryos as excess ART embryos, followed (at a later stage) by consent for a specific research project, is unnecessarily drawn out and stressful. However, the Committee noted that there are important distinctions between different purposes or intent of the research that are not known until the embryos are selected for a specific project. In addition, there are different issues to consider for research with human embryos for the purposes of improving ART services (where there is no ongoing live biological material produced from the embryos), compared with research with human embryos for the purpose of creating embryonic stem cell lines that are 'immortal' and will be used in various other ongoing research contexts. In this regard, the Committee considered that it is important for people to be fully informed about the commercial potential of their donation and, where possible, appropriate conditions should be put in place for personal use of any products of the research by the donors (such as for

treatment of children who are matched with any stem cell lines derived). Therefore, the Committee has recommended that the NHMRC Australian Health Ethics Committee should review its guidelines for consent in these circumstances.

The Committee heard that the processes that have been put in place for monitoring and facilitating compliance with the legislation are generally regarded as suitable, although suggestions for improvements to the system were also made. However, the limited powers of the inspectors appointed under the RIHE Act to monitor activities that are not covered by a licence means that suspected breaches by non-licence holders cannot be adequately investigated. The Committee has therefore recommended that the Acts should be amended to give inspectors adequate powers under both Acts to investigate suspected breaches of either Act.

Most respondents regarded the current arrangements for oversight of ART services by national and State or Territory bodies as appropriate and effective. The Committee noted that an important aspect of the accreditation arrangements is that the NHMRC ethical ART guidelines (ART Guidelines 2004[2]) are mandated in the Reproductive Technology Accreditation Committee Code,[3] a system that ensures compliance with these guidelines, including adherence to the arrangements for declaring ART embryos to be excess and for proper consent for donation of embryos for research. The latter arrangements are also included in the statutory arrangements under the RIHE Act. The Committee recommended that these arrangements are effective and should continue.

Finally, the Committee heard that the cost of the licensing arrangements are high relative to the number of licences issued and would be further increased by imposition of a cost-recovery system. Therefore, the Committee considered that it would be an unfair burden at this stage in the development of the technologies, to recover the costs of licensing from licence applicants.

Prescriptive versus regulatory legislation

Although the reviews showed that both the proponents and opponents of human embryo research would prefer to have a legislative and regulatory environment as compared with no regulatory environment, the Committee heard a number of concerns about the ability of legislation to respond to research needs in a fast-moving area of technology, leading to inevitable ambiguities in the legislation and unfair exposure of researchers to prosecution.

The Committee has recommended that certain practices, including reproductive cloning, should remain prohibited. However, to provide further protection for researchers in a rapidly developing area of technology, the Committee has recommended that the Licensing Committee should be authorised to provide rulings on interpretation of the prohibited practices as long as it reports such rulings immediately and in detail to the NHMRC and parliament.

In terms of permitted practices under the RIHE Act, the Committee has also recommended a more flexible system, where the Licensing Committee would be able to grant licences for research that is not expressly permitted by the Acts or the regulations, but is within their tenor, on condition that it reports immediately to the NHMRC and parliament, as for the prohibited practices above. Importantly, the Committee has recommended that a researcher who conducts research on the basis of a Licensing Committee ruling will be protected from prosecution.

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2. NHMRC (2004). *Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research*, NHMRC, Canberra. http://www.nhmrc.gov.au/publications/synopses/e56syn.htm
3. RTAC (2005). *Code of Practice for Assisted Reproductive Technology Units*, Fertility Society of Australia. http://www.fsa.au.com/rtac/

Such flexible regulatory arrangements may ultimately reduce the need for ongoing reviews of the Acts. However, in view of the fast-moving developments in the field, and the range of amendments proposed in these reviews, the Committee has recommended that the two Acts should be subject to a further review either six years after royal assent of the PHC and RIHE Acts or three years after royal assent to any amended legislation.

Trade and international exchange of human embryos, gametes and stem cells

International controversy around trade and international exchange of gametes, embryos and embryonic stem cells is related to ethical concerns about the sources and uses of these materials, the commodification of human tissues, and commercialisation of any therapeutic products derived from them. However, the Committee heard from ART consumers that the current Australian export prohibitions and custom regulations regarding human embryos have made it difficult for couples to export their embryos overseas for their own reproductive use. The Committee has recommended that the current arrangements, which involve personal application to the Customs Minister to export embryos for personal reproductive use, should be streamlined as much as possible to make the process less stressful for ART consumers.

The Committee heard from some researchers that these arrangements had not affected their research, whereas others noted the importance of Australian researchers having access to further cell lines from overseas. There was general concern about whether such imported cell lines have been derived using practices consistent with Australian legislation. The Committee has recommended that, in light of potential scientific benefits, the import and export of ethically derived human embryo clones and human embryonic stem cells should be permitted after approval by the appropriate authority.

Biotechnology and commercialisation

There was strong support for the prohibition of trade in human gametes or embryos, or any commodification of these items, and the Committee has recommended these activities should continue to be prohibited. However, a number of submissions noted that there should be mechanisms to ensure that donors and other members of the public have access to the benefits of research and that social justice issues should be of concern at all stages of the stem cell research endeavour. While the majority of participants acknowledged such concerns, industry groups and researchers emphasised that commercialisation is an essential aspect of research and development in this area and that, without investment, new therapeutic products cannot be developed. The Committee noted that need for such commercialisation of a research was not well understood in the community.

Australia has a strong research base in human stem cell research and Australian scientists, backed by both public and private funding, have established several companies and organisations that are capable of commercial development of research outcomes. The Committee has recommended that commercialisation of research in this area should be supported in order to ensure that potentially beneficial products can be developed for therapeutic use. However, the donors of tissue that will result in an immortal cell line or the possibility of future commercialisation need to understand that they will have no rights to any commercial gain because these rights will reside with the investors (that is, the developers of the commercial products). The Committee has therefore recommended that donors are informed about these matters when they make their donation.

Australian stem cell bank

Stem cell banks offer a way of facilitating research by making the stem cell lines more widely available to the international research community. Although some scientific researchers argued that an Australian stem cell bank may not be necessary because overseas stem cell banks (eg the UK cell bank) were adequate, the Committee heard overall strong support for an Australian stem cell bank in order to improve access to stem cell lines for research and to provide a quality control mechanism for stem cell research.

Fair access and equal involvement were the two main concerns about community involvement in a national stem cell bank. Some respondents were also concerned that the driving forces behind a national stem cell bank were profit and commercial outcomes. However, the Committee considered that, although commercialisation of therapeutic products would be an outcome if research is successful, stem cell banks help to keep research resources in the public domain. The Committee concluded that an Australian national stem cell bank would make stem cells, including embryonic and adult stem cells, more widely available to researchers and also limit number of embryos required for further derivation of stem cell lines. The Committee has therefore recommended that a national stem cell bank be established and that consideration be given to the feasibility of such a bank being managed by the Australian Stem Cell Centre, although other models, such as a decentralised system, could also be considered.

Many respondents, both ART consumers and ART clinics, were concerned that, following the decision to make excess ART embryos available for research, there would be no opportunity for these embryos to be used in actual research projects. While an 'embryo bank' may not have broad community support, the Committee considered that there may be potential in a national register of donated embryos, which may facilitate embryo donation for research and provide a transparent account of the number of donated excess ART embryos held. Such a register may also facilitate embryo donation to another couple.

Public education

In addition to the divergent views expressed, the Committee noted that, within the community, there was often a lack of understanding of the processes involved in prohibited or licensed research. The Committee also found that the scientific community and the public (informed by the media) frequently underestimated the likely timeframes for translation of research activity into therapeutic outcomes and that this had led to disappointment and reduced public trust in science. The Committee therefore suggested that accurate presentation and reporting of research advances is critical for public engagement with this area of research. In particular, emphasis should be given to making realistic assessments of the short-term and long-term benefits of the research. The Committee has recommended that further public education and consultation programs are needed in the areas of research and development covered by the Acts.

Recommendations

National legislation

1 Clinical practice and scientific research involving assisted reproductive technologies (ART) and the creation and use of human embryos for research purposes should continue to be subject to specific national legislation.

Reproductive cloning

2 Reproductive cloning should continue to be prohibited.

Prohibitions on developing and implanting embryos

3 Implantation into the reproductive tract of a woman of a human embryo created by any means other than fertilisation of an egg by a sperm should continue to be prohibited.

4 Development of a human embryo created by any means beyond 14 days gestation in any external culture or device should continue to be prohibited.

5 Implantation into the reproductive tract of a woman of a human–animal hybrid or chimeric embryo should continue be prohibited.

6 Development of a human–animal hybrid or chimeric embryo should continue to be prohibited, except as indicated in Recommendation 17.

7 Placing a human embryo into an animal or into the body of a human apart from into a woman's reproductive tract, or placing an animal embryo into the body of a human, for any period of gestation, should all remain prohibited.

8 Implantation into the reproductive tract of a woman of an embryo created with genetic material provided by more than two people should continue to be prohibited.

9 Implantation into the reproductive tract of a woman of an embryo created using precursor cells from a human embryo or a human fetus should continue to prohibited.

10 Implantation into the reproductive tract of a woman of an embryo carrying heritable alterations to the genome should continue to prohibited.

11 Collection of a viable human embryo from the body of a woman should continue to be prohibited.

Creation of human embryos by fertilisation

12 Creation of human embryos by fertilisation of human eggs by human sperm should remain restricted to ART treatment for the purposes of reproduction.

13 Creation of human embryos by fertilisation of human eggs by human sperm to create embryos for the purposes of research should continue to be prohibited except in the situation described in Recommendation 15.

Use of excess ART embryos in research

14 Use of excess ART embryos in research should continue to be permitted, under licence, as under current legislation.

ART clinical practice and ART research

15 Research involving fertilisation of human eggs by human sperm up to, but not including, the first cell division should be permitted for research, training and improvements in clinical practice of ART.

16 Testing of human oocytes for maturity by fertilisation up to, but not including, the first cell division or by parthenogenetic activation should be permitted for research, training and improvements in clinical practice of ART.

17 Certain interspecies fertilisation and development up to, but not including, the first cell division should be permitted for testing gamete viability to assist ART training and practice.

18 The Licensing Committee should develop a simple proforma application for licences to undertake training and quality assurance activities for ART clinics.

19 Consideration should be given to the use of cytoplasmic transfer (including transfer of mitochondrial DNA), under licence, for research on mitochondrial disease and other uses to improve ART treatment.

Use of fresh ART embryos

20 An expert body should formulate objective criteria to define those embryos that are unsuitable for implantation.

21 Fresh ART embryos that are unsuitable for implantation, as defined by the objective criteria, should be permitted to be used, under licence, for research, training and improvements in clinical practice.

22 Fresh ART embryos that are diagnosed by preimplantation genetic diagnosis (according to the ART guidelines) as being unsuitable for implantation should be permitted to be used, under licence, for research, training and improvements in clinical practice.

Use of human embryos created by somatic cell nuclear transfer

23 Human somatic cell nuclear transfer should be permitted, under licence, to create and use human embryo clones for research, training and clinical application, including the production of human embryonic stem cells, as long as the activity satisfies all the criteria outlined in the amended Act and these embryos are not implanted into the body of a woman or allowed to develop for more than 14 days.

24 In order to reduce the need for human oocytes, transfer of human somatic cell nuclei into animal oocytes should be allowed, under licence, for the creation and use of human embryo clones for research, training and clinical application, including the production of human embryonic stem cells, as long as the activity satisfies all the criteria outlined in the amended Act and these embryos are not implanted into the body of a woman or allowed to develop for more than 14 days.

Use of human embryos created by activation methods not involving fertilisation of a human egg by a human sperm or somatic cell nuclear transfer

25 Creation of human embryos and human embryo clones by means other than fertilisation of an egg by a sperm (such as nuclear or pronuclear transfer and parthenogenesis) should be permitted, under licence, for research, training and clinical applications, including production

of human embryonic stem cells, as long as the research satisfies all the criteria outlined in the amended Act and these embryos are not implanted into the body of a woman or allowed to develop for more than 14 days.

26 Creation of human embryos using the genetic material from more than two people, or including heritable genetic alterations, should be permitted, under licence, for research, training and clinical applications, including production of human embryonic stem cells, as long as the research satisfies all the criteria outlined in the amended Act and these embryos are not implanted into the body of a woman or allowed to develop for more than 14 days.

27 Creation of embryos using precursor cells from a human embryo or a human fetus should be permitted, under licence, for research, training and clinical applications, including production of human embryonic stem cells, as long as the research satisfies all the criteria outlined in the amended Act and these embryos are not implanted into the body of a woman or allowed to develop for more than 14 days.

Definition of a human embryo

28 The definition of a 'human embryo' in both Acts should be changed to:

'A human embryo is a discrete living entity that has a human genome or an altered human genome and that has arisen from either:

(i) the first mitotic cell division when fertilisation of a human oocyte by a human sperm is complete; or

(ii) any other process that initiates organised development of a biological entity with a human nuclear genome or altered human nuclear genome that has the potential to develop up to, or beyond, 14 days

and has not yet reached eight weeks of development.'

Consent arrangements for the donation of embryos

29 The National Health and Medical Research Council (NHMRC) should review its guidelines in relation to consent to research on excess ART embryos, in order to clarify the consent process in relation to the following issues:

- the circumstances, if any, where those who choose to donate excess ART embryos to research may be able to choose not to be contacted at some later stage to give consent to a particular research proposal
- the circumstances, if any, where a human research ethics committee can determine that the researcher need not ask for further consent to use embryos already declared 'excess'
- the development of an appropriate form of consent that could be completed by the responsible persons for excess ART embryos shortly after the declaration that the embryos are excess
- the manner in which those who donate embryos or gametes for the creation of ART embryos may express any preference for the type of research for which the tissue will be used, once the embryo is declared excess.

30 The NHMRC should develop ethical guidelines for the use of embryos that are unsuitable for implantation for research, training and improvements in clinical practice (see Recommendations 20–22).

Egg donation

31 The current principles of consent for participation in medical research must apply to sperm, egg and embryo donors, so as to ensure that decisions are freely made.

32 The NHMRC should develop guidelines for egg donation.

33 The present prohibition of the sale of sperm, eggs and embryos should continue, but the reimbursement of reasonable expenses should continue to be permitted.

Licensing arrangements

34 The Embryo Research Licensing Committee of the NHMRC (the Licensing Committee) should continue to be the regulatory body responsible for assessing licence applications, issuing licences and monitoring compliance, as under current arrangements.

35 The role of the Licensing Committee should be extended to include assessment of licensing applications and issuing licences for any additional activities permitted, under licence (see Recommendations 14–27).

36 The Australian Parliament and the Council of Australian Governments should give urgent attention to the problem of delays in the filling of vacancies on the Licensing Committee.

37 There should be no attempt to recover the cost of administration, licensing, monitoring and inspection activities associated with the legislation from researchers at this point in time.

Monitoring powers

38 The Licensing Committee should continue to perform its functions in relation to licences and databases for research permitted by licences under the Research Involving Human Embryos Act.

39 Licensing Committee inspectors should be given powers, under the Prohibition of Human Cloning Act and the Research Involving Human Embryos Act, of entry, inspection and enforcement in relation to non-licensed facilities in the same manner and by the observance of the same procedures as applicable to search warrants under Commonwealth legislation, if such powers do not clearly exist.

Oversight of ART clinical practice and research

40 There should be a continuation of the role of the Reproductive Technology Accreditation Committee in the regulation of ART.

Import and export of human reproductive materials for personal use

41 The import or export of a patient's reproductive material, including ART embryos, for the purpose of that person's ongoing ART treatment should not require any regulation other than that required under existing quarantine regulation.

Trade and international exchange of human reproductive materials and stem cells

42 The import or export of ethically derived viable materials from human embryo clones should be permitted after approval by the appropriate authority.

43 The existing requirements for the import and export of human biological materials are satisfactory and, for ethically derived human embryonic stem cells, no further restrictions are necessary.

Biotechnology and commercialisation

44 Trade in human gametes or embryos, or any commodification of these items, should continue to be prohibited.

45 Donors of tissue that is going to result in an immortal stem cell line should be informed by means of processes monitored by human research ethics committees about the potential use of that stem cell line, including the potential for commercial gain and the fact that they may not have any rights in potential stem cell developments.

46 The development of biotechnology and pharmaceutical products arising from stem cell research should be supported.

National stem cell bank

47 A national stem cell bank should be established.

48 Consideration should be given to the feasibility of the Australian Stem Cell Centre operating the stem cell bank.

49 A national register of donated excess ART embryos should be established.

Regulatory approach to legislation

50 The Licensing Committee should be authorised under the Prohibition of Human Cloning Act to give binding rulings on the interpretation of that Act, or the regulations made under that Act, on condition that it reports immediately and in detail to the NHMRC and to parliament on such rulings.

51 The Licensing Committee should be authorised by the Research Involving Human Embryos Act to give binding rulings and to grant licences on the basis of those rulings for research that is not within the literal wording of the Act, or the regulations made under the Act, but is within their tenor, on condition that the Committee reports immediately and in detail to the NHMRC and to parliament on any rulings it gives, or any licences it grants, in that way.

52 A researcher who conducts research on the basis of a ruling or a licence should be protected from liability under the legislation, provided that they act in accordance with the relevant ruling or licence.

53 In view of the fast-moving developments in the field, and the range of amendments proposed herein, the two Acts should be subject to a further review either six years after royal assent of the current Acts or three years after royal assent to any amended legislation.

Public education

54 There should be ongoing public education and consultation programs in the areas of science that are relevant to the Acts.

Abbreviations

ART	assisted reproductive technology
AS cell	adult stem cell
ASCC	Australian Stem Cell Centre
BA	Biotechnology Australia
BESST	birth emphasising successful singleton at term
BMS cell	bone marrow stromal cell
COAG	Council of Australian Governments
DNA	deoxyribonucleic acid
DTU	Diabetes Transplant Unit (Prince of Wales Hospital, Sydney)
EG cell	embryonic germ cell
ES cell	embryonic stem cell
FSH	follicle stimulating hormone
GIFT	gamete intrafallopian transfer
GMP	good manufacturing practice
hESC	human embryonic stem cell
HREC	human research ethics committee
ICSI	intracytoplasmic sperm injection
ITA	Infertility Treatment Authority
IVF	in vitro fertilisation
IVM	in vitro maturation
NHMRC	National Health and Medical Research Council
PGD	preimplantation genetic diagnosis
PHC Act	Prohibition of Human Cloning Act 2002
RCT	randomised controlled trial
RIHE Act	Research Involving Human Embryos Act 2002
RTAC	Reproductive Technology Advisory Committee
SACRT	South Australian Council on Reproductive Technology
s	section (of Acts)
SCNT	somatic cell nuclear transfer
WARTC	Western Australian Reproductive Technology Council

See the Glossary at the end of this document for definitions of terms used.

PART A
Background

1 Introduction to the reviews

1.1 Historical context

During the 1990s, research in assisted reproductive technology (ART) and human stem cells raised some new challenges. New techniques for creating a human embryo became possible, the creation of 'Dolly' the sheep in 1997 raised the possibility that cloning a human may become technically feasible, and research interest in cells taken from inside human embryos (so-called 'embryonic stem cells') increased. These developments raised significant ethical questions about how human embryos might be created, what forms of human reproduction are acceptable, and whether human embryos should be used for research.

In the late 1990s, there was no nationally consistent legislation to regulate these issues in Australia. Three States (Victoria, South Australia and Western Australia) had introduced legislation relating to ART practice, prohibiting certain practices and regulating research involving embryos and/or eggs and sperm (gametes), but the other States and Territories had no such legislation (see Section 2.5 for further information on State and Territory legislation).

In 1999, an inquiry into these issues was set up by the House of Representatives Standing Committee on Legal and Constitutional Affairs. The standing committee, chaired by Mr Kevin Andrews MP, released its report, *Human Cloning: Scientific, Ethical and Regulatory Aspects of Human Cloning and Stem Cell Research*, in August 2001 (HRSCLCA 2001). After the release of the report, the Council of Australian Governments (COAG) considered the issues in depth. In 2002, COAG agreed that the Australian Government and State and Territory governments should:

- introduce nationally consistent legislation to ban human cloning and some other, related practices considered to be unacceptable
- regulate research involving human embryos that had been created for ART treatments but were no longer required for treatment ('excess ART embryos').

The Prohibition of Human Cloning and Research Involving Human Embryos Bill was introduced into the Australian Parliament in June 2002. After initial debate, the Bill was split into two parts. Following further intensive debate, two Acts were passed and received Royal Assent on 19 December 2002:

- the *Prohibition of Human Cloning Act 2002* (PHC Act)
- the *Research Involving Human Embryos Act 2002* (RIHE Act).

Each Act included a requirement for an independent review of its operation. The reviews were to be undertaken during 2005 (the third year after the Acts received Royal Assent).

1.2 Appointment of the Legislation Review Committee

In June 2005, the Minister for Ageing, the Hon Julie Bishop MP, who has portfolio responsibility for human cloning and stem cell research, appointed the six-member Legislation Review Committee ('the Committee'). The Committee was chaired by former Federal Court judge, the Hon John Lockhart AO QC. The other members were Associate Professor Ian Kerridge (New South Wales), a clinical ethicist; Professor Barry Marshall (Western Australia), a specialist gastroenterologist and community advocate; Associate Professor Pamela McCombe (Queensland), a clinical neurologist; Professor Peter Schofield (New South Wales), a neuroscientist; and Professor Loane Skene (Victoria), a lawyer and ethicist (see Appendix 1 for further details). In accordance with the statutory requirements of both Acts, the appointments were agreed to by each State and Territory.

1.3 Terms of reference

The Minister for Ageing provided the Committee with terms of reference for the reviews of both Acts, and the National Health and Medical Research Council (NHMRC) Chief Executive Officer provided terms for the review of the RIHE Act. The Committee was required to submit its reports before 19 December 2005, the third anniversary of the day on which the two Acts received Royal Assent. This document contains the Committee's reports (see Section 1.5).

Requirements of the Acts

Section 25 of the PHC Act and section 47 of the RIHE Act set out the statutory requirements for the independent reviews. The requirements are as follows for the review of the PHC Act; different wording for the review of the RIHE Act is included in square brackets:

(1) The Minister [NHMRC] must cause an independent review of the operation of this Act to be undertaken as soon as possible after the second anniversary of the day on which this Act received the Royal Assent.

(2) The review is to be undertaken by persons chosen by the Minister, with the agreement of each State. [The review must be: (a) undertaken by the persons who undertake the Prohibition of Human Cloning Act review; and (b) undertaken concurrently with the Prohibition of Human Cloning Act review.]

(3) The persons undertaking the review must give the Council of Australian Governments and both Houses of the Parliament a written report of the review before the third anniversary of the day on which this Act received the Royal Assent. [The report must accompany the report of the Prohibition of Human Cloning Act review.]

(4) The persons undertaking the review must consider and report on the scope and operation of this Act taking into account the following:

(a) developments in technology in relation to assisted reproductive technology;

(b) developments in medical research and scientific research and the potential therapeutic applications of such research;

(c) community standards;

(d) the applicability of establishing a National Stem Cell Bank.

(5) The report must contain recommendations about amendments [if any] that should be made to this Act, having regard to the matters mentioned in subsection (4).

(6) The persons undertaking the review must consult:

(a) the Commonwealth and the States; and

(b) a broad range of persons with expertise in or experience of relevant disciplines

and the views of the Commonwealth, the States and the persons mentioned in paragraph (b) must be set out in the report to the extent that it is reasonably practicable to do so.

Terms supplied by the Minister for Ageing

The full terms of reference provided to the Committee by the Minister for Ageing are shown below:

1. The Legislation Review Committee — *Prohibition of Human Cloning Act 2002* and the *Research Involving Human Embryos Act 2002* — is required to consider and report on the scope and operation of each of the *Prohibition of Human Cloning Act 2002* and the *Research Involving Human Embryos Act 2002* taking into account:

   (i) the following statutory requirements:

   a) developments in technology in relation to assisted reproductive technology;

   b) developments in medical research and scientific research and the potential therapeutic applications of such research;

   c) community standards;

   d) the applicability of establishing a National Stem Cell Bank; and

   (ii) the following additional matters in relation to the national legislative scheme:

   a) consideration of relevant aspects of State and Territory legislation corresponding to the *Research Involving Human Embryos Act 2002*;

   b) the role played by State and Territory statutory bodies that regulate assisted reproductive technology (ART) treatment as well as the role of national organisations including, but not necessarily limited to, the Fertility Society of Australia and its Reproductive Technology Accreditation Committee (RTAC);

   c) the effectiveness of monitoring and compliance under the *Research Involving Human Embryos Act 2002* in particular, but also in relation to the *Prohibition of Human Cloning Act 2002* to the extent that issues may arise in relation to the latter Act;

   d) the ongoing appropriateness and effectiveness of changes to the Customs regulations to regulate the export of human embryos derived through ART and the import of viable materials derived from human embryo clones;

   e) options for regulation of the import and export of human embryonic stem cells;

   f) the implications of cost recovery; and

   g) implications for Australian science and economic activity.

2. The Legislation Review Committee is required to consult the Commonwealth, the States, the Australian Capital Territory and the Northern Territory and a broad range of persons with expertise in or experience of relevant disciplines.

3. The reports must, to the extent that it is reasonably practicable, set out the views of the Commonwealth, the States and Territories and those other persons consulted.

4. Each report must contain recommendations about amendments, if any, that should be made to the *Prohibition of Human Cloning Act 2002* and the *Research Involving Human Embryos Act 2002*, whichever is applicable.

5. The Legislation Review Committee is required to give a written report to the Council of Australian Governments and both Houses of the Parliament on the independent review of the operation of the *Prohibition of Human Cloning Act 2002* no later than Monday 19 December 2005. The Legislation Review Committee is required to give a written report to the Council of Australian Governments and both Houses of the Parliament on the independent review of the operation of the *Research Involving Human Embryos Act 2002* as an accompanying report to the report on the review of the operation of the *Prohibition of Human Cloning Act 2002*.

1.4 Support and resources

A secretariat consultancy, Secretariat Australia Pty Ltd, was contracted by the Department of Health and Ageing[4] to support the Committee in its task. This included the development of a consultation schedule, management of committee meetings, facilitation of hearings, receipt of submissions, management of a website, and the provision of technical writing services. The department also engaged a media consultancy, McNiece Communications Pty Ltd, to provide public relations support for the Committee. Further details are included in Appendix 1.

1.5 Reports of the reviews

This document includes the Committee's reports for reviews of both the PHC Act and the RIHE Act. The reports have been produced concurrently, as specified by the statutory requirements of both Acts and the terms of reference for the reviews. The reports have been combined because there is significant overlap between the two Acts, and the Committee's recommendations link across the overlapping areas.

The document is in three parts. Part A provides background information and describes the Committee's approach to the reviews. Part B contains a summary of information gathered in the reviews and considered by the Committee for the issues referred to in the terms of reference and for the scope and operation of the Acts. The Committee's view on these issues and its recommendations are in Part C.

4. The Department of Health and Ageing, represented by the National Health and Medical Research Council Human Cloning and Embryo Research Acts Review Support Section.

2 Overview of legislation and related issues

This chapter provides a brief overview of the two Acts, some information on the relationship between federal and State/Territory powers and on State and Territory legislation before and after the introduction of the Acts, and information about other, related matters of relevance to the reviews.

The Issues Paper prepared by the Committee includes some further explanation of these issues (see Section 3.2 and Appendix 2).

2.1 Prohibition of Human Cloning Act

The PHC Act prohibits the creation, placing in a human body or the body of an animal, import or export of a human embryo clone, whether or not it survives or can survive.

A 'human embryo clone' is defined as a human embryo that is 'a genetic copy of another living or dead human'. The definition does not include human embryos created by the fertilisation of a human egg by a human sperm (that is, identical twins). To demonstrate that a prohibited practice has occurred, it is not necessary to establish that the copy is an identical genetic copy, only that the set of genes in the nuclei of the cells of a living or dead human has been copied.

'Human embryo' is defined in the both the PHC Act and the RIHE Act as a live embryo that has a human genome or an altered human genome and that has been developing for less than eight weeks since the appearance of two pronuclei or the initiation of its development by any other means (not including any period when its development was suspended for any reason).[5]

The Explanatory Memoranda published at the time that the Bills were debated in parliament further indicated that the phrase 'initiation of development by any other means' includes any means by which the development of an embryo can be initiated, including (but not restricted to) nuclear transfer and parthenogenetic activation[6] of an oocyte:

> It is possible that a human egg could be mechanically or chemically stimulated to undergo spontaneous activation and exhibit some of the characteristics of a fertilised human egg. A parthenogenetic human embryo has the capacity to continue its development in a similar manner to a human embryo created by fertilisation.[7]

The PHC Act also prohibits the following other practices:

- creating a human embryo by a process other than by fertilisation of a human egg by a human sperm, or intentionally developing such an embryo
- creating a human embryo outside the body of a woman for any purpose apart from attempting to achieve a pregnancy
- creating or developing any of the following embryos:
  - a human embryo with genetic material from more than two people
  - a human embryo created using precursor cells from a human embryo or fetus

5. Unless otherwise stated, for the remainder of this document the term 'human embryo' has this meaning.
6. A parthenogenetic embryo is an oocyte that has been activated to start embryonic development without fertilisation by a sperm.
7. Parliament of the Commonwealth of Australia, Senate (2002). Prohibition of Human Cloning Bill, Revised Explanatory Memorandum. http://parlinfoweb.aph.gov.au/piweb//view_document.aspx?TABLE=OLDEMS&ID=1310

  - a human embryo in which the genome has been altered in any way that could be inherited by the descendants of the embryo
  - a chimeric or hybrid embryo
- developing a human embryo outside the body of a woman for more than 14 days, excluding any period when development is suspended
- collecting a viable human embryo from the body of a woman.

Embryos created or obtained using any of the above practices are collectively referred to in the PHC Act as 'prohibited embryos'. Import or export of prohibited embryos is banned, as is placing such embryos into the body of a woman.

The following practices are also prohibited:

- placing a human embryo in the body of an animal or an animal embryo in the body of a human
- placing a human embryo in the body of a human except in a woman's reproductive tract
- commercial trading in human eggs, sperm or embryos (not including the payment of reasonable expenses in connection with the supply).

Offences

Under the PHC Act, creating, developing, placing, importing or exporting a human embryo clone carries a maximum penalty of 15 years imprisonment. Other offences carry a maximum penalty of 10 years imprisonment.[8]

2.2 Research Involving Human Embryos Act

The RIHE Act sets out a regulatory framework for research on human embryos in Australia. The legislation restricts such use to those embryos that have been created in order to achieve a pregnancy but which, after a period of frozen storage, are no longer needed for this purpose (for example, because couples have completed their families).

An 'excess ART embryo' is defined as a human embryo that was created by ART for use by a woman to become pregnant but is no longer required for this purpose (that is, there is a written authority to this effect signed both by the woman for whom the embryo was created and by her spouse, if any, at the time the embryo was created).

The legislation has three main provisions:

- Use of a human embryo that is not an excess ART embryo is **prohibited** for any purpose other than for the ART treatment of a woman to achieve a pregnancy and carried out by an accredited ART centre.
- Use of an excess ART embryo, including for research, training and quality assurance activities, is **allowed** if authorised by a licence from the Embryo Research Licensing Committee of the NHMRC (see below). These activities require 'proper consent' from all 'responsible persons'.

8. Since the introduction of the legislation, no prosecutions have been made.

- Use of an excess ART embryo is **allowed** without a licence for certain 'exempt uses'. These are storage, removal from storage, transport, observation, allowing the embryo to succumb, donation to another woman to achieve a pregnancy and, in cases where the embryo is biologically unfit for implantation, diagnostic investigations by an ART centre that directly benefit the woman for whom the embryo was created in future attempts at conception. Exempt activities require consent in accordance with arrangements for the clinical practice of ART.

Under the RIHE Act, researchers or practitioners who wish to use excess ART embryos for research or any other purpose (apart from the exempt uses), must obtain a licence from the Embryo Research Licensing Committee of the NHMRC. The Act sets out the conditions that need to be met before a licence can be granted and the regulatory arrangements for managing the licensing process.

Licensing arrangements

Establishment of the Embryo Research Licensing Committee

The RIHE Act sets out a regulatory framework for the Embryo Research Licensing Committee as a principal committee of the NHMRC (referred to in this document as the Licensing Committee). The nine members of the Licensing Committee are appointed by the Australian Government minister with portfolio responsibility for human cloning and embryo research, in consultation with the States and Territories. The functions of the committee are to consider licence applications for research on excess ART embryos and to grant licences for research that meets the requirements of the Act.

The Licensing Committee must also:

- provide reports to the Australian Parliament at least every six months about its activities and any licences granted
- maintain a public database of licences that have been granted, with the name of the licence holder, a short statement of the project, any licence conditions, the number of excess ART embryos authorised, and the date and period of the licence
- appoint inspectors for monitoring and compliance (the RIHE Act also establishes the obligations and monitoring powers of inspectors).

Confidential commercial information must not be disclosed by Licensing Committee members (or others who have access to it) to anyone except those involved in the functions of the Act.

Issuing of licences

In issuing a licence, the Licensing Committee must be satisfied that the proposal includes a protocol for obtaining proper consent for the proposed use of excess ART embryos from all responsible persons, and for managing any restrictions on the consent (see 'Consent process' below for further information on consent).

Before the Licensing Committee can consider an application, the research proposal must be assessed by a human research ethics committee (HREC) using guidelines set out in the *National Statement on Ethical Conduct in Research Involving Humans* (NHMRC 1999; referred to in this document as the National Statement). The HREC assessment must be submitted to the Licensing Committee with the research proposal. Although the Act requires the Licensing Committee to consider the HREC assessment and the relevant NHMRC guidelines (see 'Regulations' below), it also requires the committee to make an independent assessment of the proposal and to consider:

- whether the number of ART embryos is restricted to that likely to be necessary to achieve the goals of the activity or project

- the likelihood of the proposed project achieving a significant advance in knowledge or improvement in technologies for treatment, which could not reasonably be achieved by other means.

The Licensing Committee must notify its decision, including any conditions, to the applicant, the HREC and the relevant State or Territory authorities. The committee can suspend or revoke a licence if it believes that the conditions of the licence have been breached. Applicants can appeal a decision to the Administrative Appeals Tribunal.

When the Act was introduced, a 'sunset clause' (RIHE Act s46) restricted the use of excess ART embryos in research that may damage or destroy the embryo to those embryos created before 5 April 2002. This clause lapsed on 5 April 2005. Licensed researchers may now use excess ART embryos created at any time, provided the appropriate consent process has been followed.

The legislation does not regulate the use of embryonic stem cells once they have been derived under licence from an excess ART embryo or imported embryo (provided their creation was consistent with Australian law). Guidance on the use of embryonic stem cells is provided by the NHMRC Australian Health Ethics Committee[9] and overseen by the institutional HREC. If the HREC is not sure that the cell line was derived in accordance with standards operating in Australia, then the research should not be approved. These considerations do not apply to adult stem cells. Research on adult and fetal stem cells is not affected by the legislation.[10]

Consent process

Under the Act, there is a staged process for declaring an embryo excess and donating it to research. First, the woman for whom an embryo was created and her spouse at the time it was created must give written authority that the embryo is an excess ART embryo. At this time (but independently of the decision to declare the embryo excess), the couple can indicate that they are willing for their embryos to be used in research. At a later stage, before the embryo is used for a specific research project (or other licensed use), 'proper consent' for the specific proposed use must be obtained from all those who have a genetic or parental responsibility for the embryo (defined in the Act as 'responsible persons'). This consent must be obtained in accordance with the *Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research* (NHMRC 2004; referred to in this document as the ART Guidelines 2004). The ART Guidelines 2004 set out requirements for provision of information. Because the decision cannot be reversed once an embryo has been destroyed, the guidelines also require that consent for destruction of an embryo should be followed by a two-week cooling-off period during which the consent can be withdrawn.

Monitoring and compliance

Inspectors appointed by the chairperson of the Licensing Committee are responsible for monitoring compliance with the Acts, and report to the chairperson of the Licensing Committee.

Monitoring and compliance activities cover organisations licensed under the RIHE Act, as well as organisations that do not hold a licence but are undertaking activities relevant to the legislation. Inspectors are authorised to enter any premises at a reasonable time if the occupier is undertaking activities authorised by a licence. However, inspectors do not have powers to enter premises of researchers that do not hold a licence. In the event of a suspected breach of the legislation in such a case, inspectors need to refer the investigation to the Australian Federal Police for the issuing of a search warrant.

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9. Information on stem cell research, NHMRC, http://www.nhmrc.gov.au/ethics/human/issues/stemcell.htm#2
10. Since its establishment, the Licensing Committee has received nine applications. Further details are provided in Chapter 9.

Inspectors have established arrangements with the Australian Federal Police and relevant State and Territory agencies. These ensure the exchange of information, and cooperation in relation to monitoring activities and investigations of suspected breaches of both the national and corresponding State and Territory legislation.

Regulations

The RIHE Act has associated Regulations, which were first enacted in 2003. The Research Involving Human Embryos Regulations 2003 prescribe the NHMRC guidelines that the Licensing Committee must take into account when issuing and overseeing a licence. These are currently:

- the ART Guidelines 2004 (*Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research*, issued by the NHMRC in 2004)[11]
- the National Statement (*National Statement on Ethical Conduct in Research Involving Humans*, issued by the NHMRC in 1999).

The Regulations also include a list of the organisations from which members of the Licensing Committee can be appointed.

Offences

Offences under the RIHE Act carry a maximum penalty of five years imprisonment.[12]

2.3 Oversight of ART clinical services and research

Since the late 1980s, clinics providing ART services have been accredited by the Reproductive Technology Accreditation Committee (RTAC), which was established in 1987 by the Fertility Society of Australia. Accreditation requires adherence to a code of practice developed by the profession. The current edition of the code (*Code of Practice for Assisted Reproductive Technology Units*) was issued by RTAC in 2005, and is referred to in this document as the RTAC Code 2005.

Since 1996, ART providers, as well as publicly and privately funded research involving ART, have also been expected to comply with the NHMRC ethical guidelines for ART (currently the ART Guidelines 2004). The RTAC Code 2005 makes adherence to the ART Guidelines 2004 mandatory.

Individual States and Territories also have specific regulatory arrangements and/or guidelines for the oversight of ART clinical practice and research. Three States (Victoria, South Australia and Western Australia) have specific ART legislation (see Section 2.5), administered by the Victorian Infertility Treatment Authority, the South Australian Council on Reproductive Technology and the Western Australian Reproductive Technology Council, respectively. In other States and Territories, some aspects of ART practice are covered by legislation, such as the *Human Tissue Act 1983* (NSW) and the *Surrogate Parenthood Act 1988* (Qld), but in these cases there is no national legislation or regulatory agency.

11. When the Act was passed in 2002, the previous edition of the ART guidelines (*Ethical Guidelines on Assisted Reproductive Technology*, issued by the NHMRC in 1996) was prescribed in the Regulations but was under revision by the Australian Health Ethics Committee. The revised edition was published in 2004, and the Regulations were amended in 2005 to take this into account.
12. Since the introduction of the legislation, no prosecutions have been made.

2.4 Import, export and trade of embryos, gametes and stem cells

Human embryos and gametes

Quarantine arrangements for the import of human embryos, sperm and eggs are managed by the Australian Quarantine and Inspection Service. These items can be imported for human therapeutic use (including implantation), artificial insemination or in vitro fertilisation (IVF). However, it is an offence under the PHC Act to import or export a 'prohibited embryo' (that is, one that is not permitted to be created in Australia).

Following the introduction of the two Acts in December 2002, the Customs (Prohibited Exports) Regulations 1956 were amended in February 2003 to prohibit the export of human embryos. However, in March 2003, further amendments were made to the Regulations to allow the Minister for Customs to consider an application for export of a human embryo for the sole purpose of implantation in the prospective mother or a relevant woman (as described in the Regulations) to achieve her pregnancy. An application may only be made to the minister by the prospective mother or, in the event that the prospective mother has died, the spouse of the prospective mother at the time that the embryo was created or donated. These arrangements are in place until July 2006.

Trading in human embryos (and human sperm and eggs) is prohibited in Australia under the PHC Act.

Embryonic stem cells

Stem cell lines, once developed, are not reproductive materials and are not covered by the above arrangements. However, the Customs (Prohibited Imports) Regulations 1958 were amended in February 2003 to prohibit the import of viable materials derived from human embryo clones because they are a byproduct of a process (human cloning) that is prohibited in Australia. The Customs (Prohibited Exports) Regulations (see above) prohibit the export of human fluids, cells and tissues if the internal volume of the immediate container in which the material is packed exceeds 50 millilitres. This provision means that most cell lines can be exported legally, as the vials used are well under the volume limit.

2.5 Legislation in Australia

The PHC Act and the RIHE Act have provided the statutory framework for States and Territories to introduce nationally consistent legislation for research involving human embryos, as agreed by COAG in 2002. Before the introduction of the national legislation in December 2002, only three States had legislation covering the clinical practice of ART and research involving gametes and embryos:

- Victoria — *Infertility Treatment Act 1984, 1995*
- Western Australia — *Human Reproductive Technology Act 1991*
- South Australia — *Reproductive Technology Act 1988* and Reproductive Technology (Code of Ethical Research Practice) Regulations 1995.

This legislation was mainly focused on ART practice, providing regulations for aspects such as storage of embryos and their destruction after a set period (which differed from State to State). Research that destroyed or diminished the potential for an embryo to be re-implanted was prohibited in all three States. Each State also banned human cloning (although 'cloning' and/or 'clone' were defined differently in each State).

The original Victorian legislation (1984) had a strict regulatory system that included criminal penalties, but this was replaced in the later Act (1995) by a licensing system for ART clinics and providers. The South Australian and Western Australian legislation also included licensing systems and codes of practice for ART providers that were slightly more permissive about research activities.

The introduction of the RIHE Act in 2002 allowed destructive research on human embryos to occur for the first time in Victoria, South Australia and Western Australia within a highly regulated framework. In the remaining jurisdictions, human embryo research had been permitted before December 2002 as no legislation had existed. Therefore, the situation became considerably more restrictive within those jurisdictions after the introduction of the national legislation.

In Victoria, the situation was complicated because, although research on human embryos was not allowed under the State Act, that Act defined a human embryo as starting from the slightly later stage of syngamy (compared with the appearance of two pronuclei, as is specified in the RIHE Act). Therefore, ART research involving fertilisation of an egg with sperm and development to the pronucleus stage, which was legal in Victoria before December 2002, was no longer permitted after introduction of the national legislation. This is discussed in more detail in Chapters 4 and 8.

Since the introduction of the national legislation, all the States and the Australian Capital Territory have enacted revised or new legislation to reflect the RIHE Act and the PHC Act, in accordance with the COAG agreement of April 2002 (see Section 1.1). For the purposes of the RIHE Act s7, the Australian Government has declared the following aspects of State and Territory legislation (by notice in the Commonwealth *Gazette*) to be a corresponding State law.

- **South Australia —** the *Research Involving Human Embryos Act 2003* (declared corresponding on 5 November 2003)
- **Queensland —** the *Research Involving Human Embryos and Prohibition of Human Cloning Act 2003* (declared corresponding on 24 March 2004)
- **New South Wales —** the *Research Involving Human Embryos (New South Wales) Act 2003* (declared corresponding on 21 July 2004)
- **Tasmania —** the *Human Embryonic Research Legislation Act 2003* (declared corresponding on 21 July 2004)
- **Australian Capital Territory —** the *Human Cloning and Embryo Research Act 2004* (declared corresponding on 22 September 2004)
- **Victoria —** Part 2A and section 166 (and relevant provisions of Part 1) of the amended *Infertility Treatment Act 1995* (declared corresponding on 27 October 2004)
- **Western Australia —** Part 4B and relevant provisions in Division 1 of Part 1 of the amended *Human Reproductive Technology Act 1991* (declared corresponding on 14 December 2005).

In the Northern Territory, the legislation had been drafted but had not passed through the Northern Territory Parliament by the time the Legislation Review process began in June 2005. The Committee was advised by officers of the Northern Territory Government that legislation in the Northern Territory remains in draft pending the outcome of the reviews of the Commonwealth legislation.

The Committee has considered corresponding State and Territory legislation within the context of its assessment of the scope and operation of the RIHE Act but decided not to consider any minor administrative differences that exist between the Commonwealth legislation and some State legislation.

2.6 International legislation and regulation

Regulation of human cloning, embryo research and stem cell technologies occurs at three levels — international, regional and national. It also occurs through other mechanisms such as ethical committee review processes and professional standards that may or may not derive their authority from legislation.

In March 2005, the United Nations adopted, by split vote, a declaration by which Member States would be called on to prohibit *all* forms of human cloning because they are incompatible with human dignity and the protection of human life. The vote was split (84 for, 34 against, 37 abstentions) as many Member States wanted to allow the practice of nonreproductive cloning in the future, if they did not already do so. Many Member States do not feel that the convention is valid and do not feel bound by it.

The Council of Europe's Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine, otherwise known as the Oviedo Convention, was opened for signature in 1997. It has been ratified by 19 of the 46 members. Amongst its many provisions, it prohibits the 'creation of human embryos for research purposes'. An additional protocol in 1998 prohibits 'any intervention seeking to create a human being genetically identical to another human being, whether living or dead'. The Council of Europe leaves interpretation in controversial policy areas to the individual member states.

National legislation in this area is under active discussion in many countries. At the national level, some countries have legislation specifically designed to cover all or some of the issues covered by these legislative reviews. Others have adopted or interpreted existing legislation or regulations (with varying degrees of coverage), and still others are in the process of preparing such legislation and/or regulations. Some do not appear to be legislating at all.

Where a practice is provided for in legislation, this does not mean that it is necessarily permitted. Legislation in a number of countries covers both practices that are clearly prohibited (such as reproductive cloning or the creation of animal–human hybrids) and practices that are regulated (such as the creation of embryos for research purposes). Whether or not those practices are or will be permitted, or under what conditions, depends on the decisions of licensing authorities, advisory committees or ethics committees established by the legislation to fulfil these regulatory functions. Their decisions are ongoing.

The following summary is based on 45 countries whose legislation and/or regulations were reviewed as part of the literature review referred by the Minister for Ageing (see Section 3.3)

Reproductive cloning

No country has legislation that permits reproductive cloning. However, the mechanism for prohibiting reproductive cloning can be either a ban on *all* forms of human cloning, or a ban on the implantation of a human clone in a woman (thus leaving open the possibility of 'therapeutic cloning').

Research with embryos

Many countries permit the use of excess or surplus human embryos for research purposes. However, some countries restrict the research to that related to ART. A small number of countries allow research on embryos only when it is of direct benefit to the embryo, so research on surplus embryos in those countries is not possible.

Where legislation permits research with embryos, it is within constraints established by the legislation (eg consent of donors, embryos only to develop for 14 days) and overseen by processes set up or authorised by the legislation (eg ethics committees, licensing bodies).

Creation of human embryos

Only a small number of countries have legislation permitting the creation of human embryos specifically for research purposes. The practice also probably happens, but without legislative oversight, in the United States. These are also countries in which there is considerable investment in stem cell research, including Belgium, China, Singapore and the United Kingdom. In general, those countries that prohibit the creation of human embryos for research purposes also prohibit the creation of human embryo clones for research, although there are exceptions.

Use of embryonic stem cell lines

In some countries, all use of embryonic stem cell lines is prohibited in the reproductive and cloning legislation. Germany does not allow the creation of embryonic stem cell lines from either surplus or cloned embryos. However, it does permit the importation of embryonic stem cell lines and their use in research.

A number of countries permit research using embryonic stem cells from surplus human embryos, but not the creation of human embryo clones, and hence the isolation of embryonic stem cell lines from this source.

Governments also need to ensure that their ethical restrictions on research are honoured in relation to imported cell lines. While Australia deals with this through its Customs legislation, other countries manage it via guidelines and funding bodies. Canada, for example, has guidelines overseen by the National Institute of Health Research that require all imported cell lines to be derived in ways consistent with Canadian legislation.

Creation of human–animal chimeras and hybrids

Where legislation explicitly refers to the possibility of creating, developing or implanting human–animal hybrid embryos or chimeras, those practices are banned.

3 Conduct of the reviews

3.1 Introduction

To meet the statutory requirements and the terms of reference for the review, and to encourage the Australian community to discuss the legislation, the Committee considered various methods to engage the general community in discussions about the legislation and also to find out the views and experiences of the people most directly involved — scientific researchers, consumers and practitioners of ART services, and relevant government agencies.

Time constraints placed a practical limit on the consultation mechanisms available to the Committee. The Committee decided that a combination of written submissions and several styles of stakeholder meeting would provide means for collecting information on scientific developments in the area and on the values and perspectives of the community. The Committee therefore consulted extensively through the following activities:

- establishment of a review website
- written submissions
- face-to-face meetings with key stakeholders
- public hearings and some private meetings (at stakeholders' request)
- facilitated stakeholder discussion forums
- site visits.

These activities are described in more detail in Section 3.2.

In addition, the Committee reviewed the latest (2005) results of focus group and telephone survey research by the Public Awareness Program of Biotechnology Australia (see Section 3.3).

3.2 Consultations

The Committee made considerable effort to obtain a broad range of views from the following individuals and groups:

- private individuals (including those from universities, organisations and research institutions, as well as unaffiliated members of the general public)
- research organisations
- ART clinical service providers
- professional organisations, including the Fertility Society of Australia and Reproductive Technology Accreditation Committee
- Australian Government agencies and parliamentarians
- State and Territory government agencies and parliamentarians
- ethicists, lawyers and other academics
- health consumer groups
- religious groups
- other lobby groups with a known interest in these issues.

Website

To provide information to the Australian public about the reviews, a website was established in July 2005.[13] The website provided information about the Committee, the terms of reference for the reviews, links to the current legislation and other relevant websites, the Issues Paper (see below), fact sheets, guidelines for submissions, information about the public hearings, reports of the discussion forums, and copies of written submissions to the reviews (apart from those designated as confidential). The website also provided a facility for electronic lodgment of written submissions.

Interested people and organisations were invited to register their interest in the reviews on the website. Those who registered received emailed notification of developments in the reviews, including invitations to public hearings.

Issues Paper

At the start of the reviews, the Committee prepared an Issues Paper to provide specific information about the legislative reviews, promote community understanding of the current legislation, highlight some of the main issues where public and stakeholder comment would assist the Committee, and encourage people to make submissions on relevant matters.

The information in the Issues Paper was based on the current legislation and regulatory arrangements. Readers of the paper were also encouraged to read the legislation in full, as well as other material available on the Legislation Review website and on the website of the NHMRC.

A copy of the Issues Paper is included in this report as Appendix 2.

Written submissions

On 9 July 2005, the Committee published advertisements in the major national, State and Territory newspapers calling for written submissions to the reviews, with a closing date of 9 September 2005. However, submissions received after the closing date were also taken into account by the Committee.

Submissions were accepted in hard copy, and electronically via email or the Legislation Review website. Complete copies of all submissions were forwarded to the members of the Committee, who used them to inform their work. Apart from submissions that were designated as confidential, the submissions were also posted on the website. Material from the submissions has been quoted in this report.

The Committee received a total of 1035 submissions from a broad range of individuals and organisations in the following categories:

- private individuals (including researchers, health practitioners, health consumers and unaffiliated members of the public) (921 submissions)
- representatives of organisations (including research organisations, university departments, professional organisations, ART services, health consumer groups and religious groups) (98 submissions)
- government agencies (8 submissions)
- individual parliamentarians (8 submissions).

13. See http://www.lockhartreview.com.au

Of the submissions received, 345 were from New South Wales, 254 from Victoria, 180 from Queensland, 54 from Western Australia, 26 from the Australian Capital Territory, 19 from South Australia, 9 from Tasmania, 3 from the Northern Territory, and 3 from overseas. Details about location were not provided for 142 submissions.

In addition to the submissions, the inquiry received nine different standard 'form' letters and petitions. Of these, eight (with a total of 898 signatures) supported a ban on cloning and/or embryo research, and one (378 signatures) supported stem cell research. Copies of the letters and petitions can be found on the Legislation Review website.

A list of all the submissions is included in Appendix 3.

Public hearings

The Committee further consulted with stakeholders and other interested parties through public hearings. At these hearings, the Committee spoke with invited stakeholders on a one-to-one basis over a half-hour or one-hour session. The public was invited to attend most of these hearings as observers, except for a small number of sessions where stakeholders had requested a private meeting with the Committee. The public was notified about the hearings through the Legislation Review website, by email (for those who had registered through the website), and by media releases.

Hearings were held in all State and Territory capital cities. The Committee spent two days in each of Sydney (8–9 September), Brisbane (19–20 September) and Melbourne (29–30 September), and one day in each of Adelaide (1 September) and Perth (21 October). In Darwin (31 October), the Committee met with a small number of groups in private sessions. For Hobart (7 October), the Committee used a videoconference link for its consultations.

Individuals and organisations invited to address the Committee were selected on the basis of:

- the terms of reference
- advice to the Committee from relevant government agencies on stakeholders who had the greatest interest in the issues
- the Committee members' own knowledge about relevant stakeholders
- expressions of interest from stakeholders in meeting with the Committee
- information contained in written submissions.

At least three Committee members were present at each hearing, together with members of the secretariat. A recording was made of each hearing for the use of the Committee, and transcripts were produced to ensure that the Committee had an accurate and complete record of proceedings. Some quotes from the hearings are reproduced in this report.

The individuals and organisations who met the Committee in hearing-style meetings are listed in Appendix 4.

Private meetings

The Committee met privately with State and Australian Government ministers, officials from relevant State and Territory government departments, and the Embryo Research Licensing Committee of the NHMRC. The Committee also had private meetings with some individuals and organisations at their request.

Discussion forums

Facilitated discussion forums with invited participants were held during the Committee's consultation visits to Sydney, Melbourne and Brisbane. The discussion forums allowed the Committee to hear the views of a larger number of stakeholders than could be accommodated at one-to-one hearings, and to encourage discussion and debate among participants with opposing views. Those invited to attend these forums were selected on the same basis as for the hearings.

A facilitator led the discussion at each forum, which was structured around the two Acts and the Committee's terms of reference. Committee members attended the forums largely as observers, with the aim of gathering information about the issues that were of interest and concern to the invited attendees. The issues discussed at the forums were summarised and published on the Legislation Review website. Lists of the attendees at the forums are included in Appendix 5.

Site visits

The Committee visited both Sydney IVF and Monash University (which are licence holders under the RIHE Act) and met with personnel from those organisations to gain a greater understanding of the work performed by organisations directly affected by the two Acts. In Melbourne, the Committee visited the Australian Stem Cell Centre in the Monash University precinct and met personnel from that organisation, from the Monash Immunology and Stem Cell Laboratory, and from Stem Cell Sciences Ltd.

Media coverage

On 17 June 2005, the Hon Julie Bishop MP, the Australian Government minister with portfolio responsibility for the Acts, issued a media release to announce the members of the Committee. On 4 July, Ms Bishop held a well-attended media conference with the Chairperson, the Hon John Lockhart AO QC, to coincide with the first meeting of the Committee.

On behalf of the Committee, Mr Lockhart issued a media release on 26 August 2005 to announce that the Committee would be undertaking public hearings around Australia. Local and national media were alerted before the Committee visited each State and Territory. All media statements were posted on the Legislation Review website for public and media information.

Following the first public hearings in Adelaide on 1 September 2005, there was extensive national publicity. Media interest in the Committee's work peaked during public hearings held in Melbourne on 29 and 30 September 2005, which were attended by a large contingent of television, print and radio journalists. Print and radio media were also present at public hearings in Sydney and Brisbane. Moderate numbers of media inquiries were received by the Committee's media consultant over the course of the reviews.

Reports of the work of the Committee in print media and on radio have been positive, and the Committee's consultation activities were well received by participants.

The initial media release, with a call for written submissions to the reviews, is shown in Appendix 6.

3.3 Other sources of information

A recent literature review of scientific and technological advances in human cloning, human embryo research and related matters, including stem cell technologies, from December 2001 to July 2005, was referred to the Committee by the Minister for Ageing (Biotext 2005). The literature review also provided information about exchange and trade of human embryos and embryonic stem cells (including stem cell banks), and international regulation of human cloning/embryo research. This

review provided a useful information resource for the Committee, and summaries of the findings are included in several chapters of this document. Further details from the literature review, including the methods, results of the searches and all relevant scientific references, can be seen on the Legislation Review website.[14]

The Committee also drew on results, provided by Biotechnology Australia's Public Awareness Program, of research into public attitudes to stem cell technologies from focus groups and telephone surveys.[15] These results provided a useful source of information on community attitudes and standards. The Committee also had an opportunity to discuss the survey with Mr Craig Cormick, Director of the Public Awareness Program.

Finally, the Committee's discussions about the definition of a human embryo were informed by a draft discussion paper, *Human Embryo — A Biological Definition* (NHMRC 2005). This paper addressed issues concerning the definition of 'human embryo' in the current legislation that have arisen as a result of the Licensing Committee's work since 2003.

3.4 Committee meetings

The Committee met regularly during the course of the reviews. Formal committee meetings were held on 4 July, 15 July, 12 August, 18 October (by teleconference), 4 November, 18–19 November, 28 November and 4–5 December 2005. In addition, the Committee met during the consultation process in the States and Territories.

14. See http://www.lockhartreview.com.au
15. See http://www.biotechnology.gov.au

PART B
Information considered in the reviews

4 Developments in assisted reproductive technology

4.1 Background to ART research

In the late 1960s, scientists investigated the possibility of achieving fertilisation in the laboratory (in vitro) and the culture and implantation of embryos to achieve a successful pregnancy. The world's first baby using in vitro fertilisation (IVF) was born in the United Kingdom in 1978; the first Australian IVF baby was born in Melbourne in 1980. Since that time, further scientific advances have improved outcomes from IVF and enabled the development of a wider range of assisted reproductive technology (ART) techniques to help couples with a range of difficulties in having babies.

Significant technological steps have included the ability to store frozen embryos at an early stage of in vitro development,[16] and the introduction of the technique called preimplantation genetic diagnosis (PGD) to help couples with a specific genetic disease to have a baby free of the disease. The development of these techniques led to the opening of ART clinics in Australia and elsewhere.

At the time the legislation was being considered in 2001–02, ART techniques available in Australia included donor insemination, IVF, the transfer of sperm and eggs back into the woman's reproductive tract for fertilisation to occur (gamete intrafallopian transfer, or GIFT), injection of sperm directly into eggs for fertilisation (intracytoplasmic sperm injection, or ICSI), and PGD. By this time, researchers had also started to investigate new ways to create gametes or to combine genetic material to create embryos that were the genetic offspring of couples who would otherwise have to rely on donated gametes or embryos.

This chapter summarises the findings of the literature review referred by the Minister for Ageing (Biotext 2005; see Section 3.3) and the information received by the Committee during the reviews about research developments under the terms of the RIHE Act.

4.2 Literature review — developments in ART since 2001

For the literature review, the international literature relating to ART was searched from December 2001 until July 2005, and the most relevant review articles were reviewed and summarised. Further details from the literature review, including methods, results of the searches and all relevant scientific references, can be seen on the Legislation Review website.[17]

Improving ART outcomes

Methods of ART have changed in the past decade. In Australia in 1993, GIFT was used in 36% of all fresh cycles, but by 2002 this had dropped to just 1%. Conversely, ICSI was first used in the early 1990s, and by 2002 accounted for almost 50% of fresh cycles.

Despite these developments, achieving a successful pregnancy with ART remains difficult. The latest statistics published by the Australian Institute of Health and Welfare National Perinatal Statistics Unit and the Fertility Society of Australia are shown in Table 4.1

16. With the first baby born from a frozen embryo in 1983.
17. See http://www.lockhartreview.com.au

Table 4.1 Progression of fresh, non-donor ART treatment cycles, Australia and New Zealand, 2002

Stage	Number	Per cent
Cycles started	19,883	100.0
Oocyte retrievals	17,877	89.9
Embryo transfers	15,482	77.8
Pregnancies	4,739	23.8
Live deliveries	3,640	18.3

Source: Bryant J, Sullivan EA and Dean JH (2004). *Assisted Reproductive Technology in Australia and New Zealand 2002*, ART Series No. 8, Australian Institute of Health and Welfare National Perinatal Statistics Unit and the Fertility Society of Australia.

The figures shown in Table 4.1 represent averages for Australia and New Zealand and mask variation in success rates with maternal age (pregnancy rates decline with age) and between ART centres. Furthermore, it is now accepted that the safest and most desirable endpoint for ART treatment is a single, live baby born at term (gestation of 37 weeks or more). This outcome has been designated as the BESST (birth emphasising successful singleton at term) endpoint. Recalculating the figures in Table 4.1 to only show BESST outcomes gives live singleton deliveries at term as 12.9% of cycles started. Much ART research is therefore directed at achieving higher rates of BESST outcomes, as well as improving the safety and efficiency of oocyte retrieval and increasing the range of people who can benefit from ART treatment.

For this reason, active research on various aspects of ART continues throughout the world. This involves clinical trials during human fertility treatment, research on human embryos that are left over from ART treatment or available under the regulatory arrangements of the countries involved, work on animal models and other laboratory methods. The main areas of international research in relation to ART are listed below, with a brief description of the related research issues. Some of this research would not be permitted in Australia.

- Embryo culture conditions
  - Different types and combinations of nutrients are included in the culture media at different stages of embryo development, to best mimic the natural environment. However, the effects of culture media on gene expression are still unknown.
- Embryo selection and transfer
  - Traditionally, embryos were transferred at the two-day stage, but studies have suggested that extending the culture period to three days (using improved culture media) may improve clinical pregnancy rates (Oatway et al 2004). Other studies report that it is better to extend the culture period even further, by transferring selected 5–6-day-old blastocysts rather than 2–3-day-old embryos (Kolibianakis and Devroey 2002, Ebner et al 2003).
  - ART methods also traditionally relied on the transfer of multiple embryos, to optimise the chance of implantation and pregnancy. However, this increased the risk of multiple pregnancies and associated maternal and perinatal morbidity rates. Techniques are being refined to allow the transfer of single embryos without significantly compromising the efficiency of ART (Gardner and Sakkas 2003).

- Embryo development and implantation
  - Assisted hatching is a method in which the zona pellucida (the outer shell of the egg) is perforated to assist release of the embryo and to increase its chance of implanting in the uterus.
  - Cytoplasmic transfer (injecting cytoplasm from the eggs of a healthy woman into the eggs of a woman experiencing conception problems) has been used as a fertility treatment overseas. However, use of this method was stopped in 2001 because of concerns about its safety.
- Screening embryos for abnormalities
  - PGD is used to test embryos for genetic abnormalities before pregnancy is established. It is offered to both fertile and infertile carriers of single-gene disorders to increase the chance of a healthy pregnancy and decrease the need for termination. Studies indicate that the technique is efficient and safe, but PGD requires removing a sample of the embryo, and the long-term effects of decreasing the mass of an embryo by removing cells at the cleavage stage are unknown.

Novel methods of overcoming fertility problems

Currently, ART treatment uses the natural process of fertilisation of an oocyte with sperm, with the process being completed in culture in the laboratory (in vitro). However, this is not possible for women who do not produce oocytes (eggs), or men who do not produce sperm. Currently, such individuals need to use eggs or sperm donated by another person, which means that children born by this method are not genetically related to one or both of their social parents.

To overcome this problem, researchers are pursuing research to create gametes from cultured embryonic stem cells (in vitro gametogenesis), or using cell fusion and chromosome reduction methods (haploidisation). These two approaches are described briefly below.

In vitro gametogenesis

Research has improved understanding of the development path of germ cells (precursors of eggs and sperm). This has led to the ability to use embryonic stem (ES) cells to establish a population of cells very like primordial germ cells, which can differentiate into sperm or eggs.

Three studies in mice showed that:

- ES cells can differentiate into mature oocytes
- ES cells can differentiate into sperm
- sperm derived from ES cells injected into eggs can form blastocysts (although the functional quality of these gametes remains to be tested).

In 2004, researchers also showed that human ES cells can differentiate into germ cells. However, this technique has not so far produced viable embryos in humans or animals.

Somatic cell haploidisation

Some researchers are currently investigating the fusion of a gamete (egg or sperm) and a body (somatic) cell that has undergone a reduction of its chromosomes to the haploid number. (A haploid cell is one that has undergone meiotic cell division and only has one of each pair of chromosomes.) The somatic cell originates from a male or female patient who is unable to produce their own gametes.

Preliminary experiments using mouse or bovine oocytes have not been successful. For example, in a study using mouse oocytes and mouse cumulus cells, most of the resulting embryos exhibited numerous chromosomal abnormalities and did not survive (Tesarik and Mendoza 2003). Problems have included abnormalities of the somatic chromosome and spindle formation, as well as those

usually associated with nuclear transfer, such as genetic reprogramming. These problems might be overcome by selecting donor stem cells and oocytes in a different cell phase, selecting a different type of stem cell, or altering the culture media.

In vitro maturation of oocytes

Research on the maturation of oocytes was not covered by the literature review because it does not specifically involve research on embryos, which was the topic of the literature review and focus of the search terms used. However, information from submissions to the legislative review about this important area of research is included in Section 4.3.

4.3 Submissions and hearings on developments in ART

Licensed ART activities

Since the Licensing Committee was appointed in 2003, five applications have been received and licences granted for research relating to improvements in ART technology: four for research and one for training.

Many respondents to the reviews told the Committee that they were surprised to find that five of the nine licences issued since the introduction of the RIHE Act were for ART research, rather than for the extraction of embryonic stem cells and development of stem cell therapies. For example, the National Civic Council (Submission LRC246) commented that stem cell therapy was only listed as a research component in a small number of licence applications, despite it being the focus of the 2002 parliamentary debate. Queensland Right to Life also stated that:

> … out of the 705 embryos for which licences were given for the derivation of human embryonic stem cells, only 150 specifically mentioned using them for therapies [the stated use of the 2002 legislation]. *Queensland Right to Life (Submission LRC376)*

This element of surprise appears to have arisen because the intense media coverage in 2002 was about human cloning and embryonic stem cell research rather than about the use of embryos for ART research, which was already regulated in some, but not all, jurisdictions in Australia. However, the media coverage ignored the fact that ART research (and some other related research, such as studies of ovarian cancer) was already well established in most jurisdictions of Australia.

Some respondents to the reviews also commented that they were surprised that a licence had been granted to allow training of embryologists, and some stated that the Licensing Committee should not have allowed such a use under the RIHE Act because it did not contribute to a 'significant advance in knowledge or improvement in technologies for treatment' (see Section 2.2). For example:

> Nearly the entire public and parliamentary debate about the use of human embryos for research was focussed on the potential of human embryonic stem cells for therapy. However, for only 150 out of the 1735 human embryos for which licenses have been issued is stem cell therapy mentioned as a justification. In one case the license refers to the stem cells 'eventually' being used for therapies for Parkinson's and juvenile diabetes … The use of some human embryos as training tools in how to do embryo biopsy is contrary to the legislation as such a use leads neither to a significant advance in knowledge nor to an improvement in technologies for treatment. *National Civic Council (Submission LRC246)*

> … the use of 'spare embryos' in order to train IVF technicians is not, in this submission, a licit or permissible use authorised by the current regulatory regime (see s.10 *Research Involving Human Embryos Act* 2002 (Cth)). However, under the current regulatory regime, licences have been granted specifically for this purpose.
> *Shop Distributive and Allied Employees Association (Submission LRC399)*

However, as for other aspects of medical practice, ART practitioners have argued that training of embryologists and quality assurance activities are vital for the continuing provision of ART services and that both contribute to improved ART outcomes (and therefore to 'improvement in technologies'). These activities have therefore been accepted by the Australian Health Ethics Committee, institutional ethics committees and the Licensing Committee as meeting the requirement for an 'improvement in technologies for treatment'.

Details of the licences that have been issued to date for research relating to improvements in ART technology are shown in Table 4.2.

Table 4.2 Licences issued for research on development of ART

Organisation	Licence no.	No. of embryos	Licence title	Dates
Sydney IVF Pty Ltd	309701	512 (670) [a]	Improvement of laboratory conditions for embryo culture	16/4/04 – 16/4/07
Sydney IVF Pty Ltd	309702A	128 (170) [ab]	Effect of an additive on embryo culture: analysis of growth and epigenetic programming	16/4/04 – 16/4/07
Sydney IVF Pty Ltd	309702B	255 (170/85)[c]	Development of methods for preimplantation genetic and metabolic evaluation of human embryos	16/4/04 – 16/4/07
Melbourne IVF Pty Ltd	309704	120	Development of testing procedures for unbalanced chromosome errors in human embryos	16/4/04 – 16/4/07
Monash IVF Pty Ltd	309700	105 (175) [a]	Use of excess ART embryos for training in embryo biopsy	11/3/05 – 11/3/08

a Number in brackets is the number that is allowed to be thawed to obtain up to the number indicated in a suitable state for research/training.

b These embryos can also be used for research under Licence 309702B.

c In this case, 170 of the embryos must have been first used for research under Licence 309701; 85 can come from cryostorage.

Source: Database of licences authorising the use of excess ART embryos, NHMRC (http://www.nhmrc.gov.au/embryos/monitor/database/index.htm)

Detailed outcomes of the research are not available at this stage because the research is still in progress.

At its visit to Sydney IVF, the Committee heard that research has led to the development of improved culture media. (Sydney IVF has a brand of embryo culture media that is commercially available). During the visit, Professor Robert Jansen, Medical Director of Sydney IVF, also reported that improvements in embryo culture media and technology over the past few years have led to significant increases in pregnancy rates. Sydney IVF has two licences for improving culture media (see Table 4.2).

Effect of the legislation on ART research

The overwhelming response to the reviews from ART providers and researchers was that the legislation has impeded research to improve ART technologies that was active before the legislation was passed. For example, Professor HW Gordon Baker, an ART researcher from Victoria, stated:

> The inability to do human fertilisation research has impeded the improvement of clinical ART and has led to the introduction of poorly researched techniques (for example intracytoplasmic sperm injection) into clinical practice without the usual preclinical evaluation that should be undertaken to assess possible risks.
> *Professor HW Gordon Baker, Victoria (Submission LRC391)*

Respondents stressed the importance of ongoing research for the continued improvement of ART. For example, Dr Stephen Junk, the scientific director of the Hollywood Fertility Centre in Western Australia, stated:

> Results from IVF related treatments are still improving worldwide. Without further ethically approved research involving human embryos success rates will plateau. A good number of patients pursuing IVF treatment are aware of this. As they have dealt with hardships, both mentally and physically regarding their infertility, they are quick to understand that without previous research involving human embryos their current chance of success would be far reduced. Those having excess embryos in storage after completing their family will consequently often inquire about using their embryos for research.
> *Dr Stephen Junk, Western Australia (Submission LRC257)*

The Committee identified the following issues in the legislation that have clearly impeded both ART research and clinical practice:

- The definition of a human embryo in the Acts (RIHE Act s7 and PHC Act s8) starts from the appearance of two pronuclei. This prevents any research requiring experimental fertilisation of an egg with sperm because, once the two pronuclei are visible (the earliest biological marker for such research), an embryo has been created and creation of a human embryo for research contravenes the PHC Act s14. These provisions prevent a range of research to improve IVF, including maturation of oocytes, testing of sperm quality and fertilisation research.
- The inclusion of parthenogenetically activated oocytes in the definition of a human embryo clone (see Section 2.1) has made it illegal to create such an entity. This has prevented research on activated oocytes.
- The prohibition of creation of human–animal hybrid embryos (PHC Act s20), combined with the current definition of an embryo, has also prevented other research or testing requiring fertilisation (such as tests for sperm quality by fertilisation of hamster eggs).
- The prohibition of creation of a human embryo for any purpose other than to achieve a pregnancy in a woman prevents the creation and use of fresh embryos for research. As well, the provisions of the RIHE Act for declaring embryos to be excess ART embryos and giving proper consent for research have precluded the immediate (fresh) use of ART embryos.
- The prohibition of creation of a human embryo containing genetic material provided by more than two persons prevents research or clinical use of cytoplasmic transfer to assist embryonic development (particularly in older women) or to prevent mitochondrial disease.
- Lack of clarity in the definition of an excess ART embryo in the RIHE Act has created uncertainty about whether it is legal to use surplus ART embryos that are not suitable for implantation for various reasons. Such embryos would be useful for research, training and quality assurance activities.
- The inclusion of training and quality assurance as activities that require a licence has presented a significant administrative barrier to these activities.

The Committee heard that the following areas of ART research and clinical practice had been affected:

- further understanding of and improvements in IVF
- development of methods for in vitro maturation of oocytes
- development of methods for freezing ovarian tissue and oocytes
- assessment of sperm quality
- improvements to embryo culture and implantation methods
- studies of cytoplasmic transfer
- training and quality assurance.

Further details about each of these areas are provided below, as well as some information about recent international research on alternative methods of producing gametes. Testing of such methods using human materials would be prohibited in Australia under the current legislation.

In vitro fertilisation studies

Under the current definition of a human embryo, researchers are not able to undertake experimental fertilisation studies because the legislation requires the process to cease before the two pronuclei are formed — thereby preventing the researcher from confirming that fertilisation has occurred:

> In 2002, it finally became illegal throughout Australia to fertilize a human egg in order to acquire knowledge concerning the IVF process specifically, and human reproduction generally. *Sydney IVF (Submission LRC819)*

Several other submissions referred to the definition of a human embryo that was included in the *Victorian Infertility Treatment Act 1995*. This definition was superseded by the national legislation in 2002 (see Section 8.1). Under the Victorian definition, an embryo existed only after the pronuclei had fused at syngamy (just before the first cleavage division). Therefore, before this stage, the pronuclear oocyte was considered a zygote and could be used in research without contravening the legislation.

At the Melbourne hearings, Dr John McBain, Director, Melbourne IVF; Professor Louis Waller, Monash University; Ms Louise Johnson, Chief Executive Officer, Victorian Infertility Treatment Authority; and Professor Jock Findlay, Chair, Victorian Infertility Treatment Authority, told the Committee that the introduction of the national legislation had stopped research previously allowed by the Victorian legislation:

> The definition of the human embryo changed as a result of the amendment of this Act. In the previous Act it was defined that the embryo really began at what's called syngamy or after fertilisation, which then allowed research on and up to the point of fertilisation, which was quite important from the point of view of development of better ART techniques. With the amendment of the Act that's now no longer possible … From a legal perspective in terms of our role in administering the Act it works fine but we think that in terms of improving ART procedures, which is one of the things that ITA should be facilitating, then that's now been restricted in that you just can't do the sorts of things that need to be done to improve fertilisation. *Professor Jock Findlay, Chair of the Victorian Infertility Treatment Authority (Melbourne hearings)*

The potential of research using fertilisation up to the point of syngamy was also noted by Professor HW Gordon Baker, an ART researcher in Victoria, who told the Committee that fertilisation research up to syngamy could improve methods of cryopreservation of oocytes and ovarian tissue, and help patients undergoing chemotherapy or radiotherapy, which can cause infertility (Supplementary submission LRC391).

However, others objected to the use of syngamy in the definition of embryo:

> The zygote is not a pre-embryo but the first cell in the line of embryogenesis. About 20 hours after this event occurs, the chromosomes align themselves for the first cell division. This is not syngamy as biologists know it and there is no such thing as a pre-embryo. But the scientists knew that there was an intuitive repugnance to experimentation on the zygote and so invented a being somewhere between a gamete, with no moral significance, and an embryo with great moral implications.
> *Dr Joseph Santamaria, President, Family Council of Victoria (Submission LRC381)*

Chapter 8 includes further discussion of the definition of a human embryo, including an explanation of the previous Victorian legislation.

In vitro maturation of oocytes

At the Adelaide hearings, the Committee heard from Associate Professor Jeremy Thompson, Deputy Director, Research Centre for Reproductive Health, University of Adelaide, about research to develop the technology of 'in vitro maturation' (IVM) of oocytes.

This method involves the culture of immature oocytes in the laboratory under conditions designed to allow full maturation. Immature oocytes can be obtained from previously frozen ovarian tissue samples or retrieved using the same methods used to obtain mature oocytes; that is, with the use of transvaginal ultrasound guidance equipment to remove immature follicles from the ovaries. Associate Professor Thompson and others explained that this technology would be a significant advance over current methods because, unlike mature sperm, mature oocytes are difficult to freeze and have to be obtained fresh for each fertilisation cycle.

To obtain mature oocytes, women are given follicle stimulating hormone (FSH) to stimulate maturation of oocytes in the ovaries. After daily monitoring of hormone levels, the mature eggs are collected at ovulation. This process is costly and time consuming. Further, if excess FSH is given, this can lead to a dangerous (potentially fatal) condition called ovarian hyperstimulation disorder. Because IVM does not require as much FSH treatment, it reduces the risks to women (as well as the time and cost) of this aspect of ART treatment. At the Adelaide hearings, Associate Professor Thompson described the benefits of IVM:

> … the reason why it is an attractive offering is that there are risks to the woman receiving large doses of gonadotrophin to a syndrome called ovarian hyperstimulation syndrome, which can actually lead to death in very rare cases and also to quite significant lengths of hospitalisation. So in vitro maturation would offer health advantages to women receiving treatment through IVF and also substantially reduce costs, because gonadotrophins are a large cost associated with the IVF cycle. *Associate Professor Jeremy Thompson, Deputy Director, Research Centre for Reproductive Health, University of Adelaide (Confidential submission LRC266; reproduced with permission of the author)*

Furthermore, for some women with polycystic ovarian syndrome, it is not possible to obtain mature oocytes. Finally, IVM would provide a means of developing mature oocytes from frozen ovarian tissue stored by women who undergo chemotherapy or other therapies that will result in loss of ovarian tissue.

> Certainly we have numerous patients who are relying on that being developed, largely women who have had ovarian cortex stored before chemotherapy or radiotherapy for malignant disease, and the best way some of them are going to ever use that tissue to reproduce will be when in vitro maturation from those primordial follicles in that ovarian cortex through to mature oocytes is perfected. So just from a straight infertility patient therapeutic view, that would be invaluable technology … if we can do in vitro maturation we may well be able to use a lot less super ovulatory drugs and that would benefit the health budget no end and reduce one of the side effects of ART treatment.
> *Dr Keith Harrison, Scientific Director, Queensland Infertility Group (Brisbane hearings)*

However, IVM is a complex procedure in which both the nucleus and the cytoplasm of the oocyte need to be brought to precisely the right point of maturity to allow fertilisation with a sperm. Perfecting this technique requires detailed investigation of the chemical and cellular processes involved in the maturation of oocytes to find out if oocytes matured in vitro are fully competent and able to undergo fertilisation and embryonic activation:

> Specifically, it is presently not allowable to investigate how immature human eggs (obtained without the use of stimulatory drugs) might best be matured in the laboratory.
> *Sydney IVF (Submission LRC819)*

Associate Professor Thompson told the Committee that more than 300 children have already been born by IVM worldwide. However, without proper research to ensure that IVM oocytes achieve the same outcome of fertilisation as naturally matured oocytes, there are safety implications for people born as a result of this technology:

> In vitro maturation has been widely practised in animal models, most specifically in the mouse as a research tool and in sheep, cattle, pig and deer and horses for both research purposes and … for the purposes of breeding. Furthermore, in vitro maturation is also practised for some applications of species conservation. Internationally, the practice of ART is changing with the incorporation of in vitro maturation as a routine procedure to provide a cost efficient alternative to in vitro fertilisation. However, current efficiencies in terms of embryo yield and subsequent implantation rates following transfer are, at best, approximately ½ that of routine IVF. Furthermore, the overall health of IVM conceived children remains unknown.
> *Associate Professor Jeremy Thompson, Deputy Director, Research Centre for Reproductive Health, University of Adelaide (Confidential submission LRC266; reproduced with permission of the author)*

Dr John McBain, Director, Melbourne IVF, told the Committee that the biggest effect of the Act has been prevention of work on in vitro maturation of oocytes from frozen ovarian tissues. These oocytes cannot be fertilised under the current definition of embryo, because the legislation requires the process to cease just before the two pronuclei are formed — thereby preventing the researcher from confirming fertilisation:

> The one thing which has the greatest impact on our group and our research … was to stop in its tracks the work that we were doing on the development of mature eggs from frozen pieces of ovarian tissue. In my group … through placing pieces of frozen then thawed ovarian tissue on the kidney capsule of the immunologically suppressed mouse, we would be able to grow human eggs. We were stopped from being able to fertilise these eggs because of the redefinition of the term 'embryo' in the federal legislation. Up until then, under the quite arduous Victorian legislation, we had a window of being able to fertilise an egg which had been going in that way, and that was stopped completely. So I have a continuing concern about the unintended consequences of any form of legislation … we would be happy, if there needs to be any definition at all in terms of reproduction, at post syngamy as it was in the Victorian Act.
> *Dr John McBain, Director, Melbourne IVF (Melbourne hearings)*

The Committee heard that another method to test the activation potential of mature human oocytes is to induce parthenogenetic activation of the mature oocytes:

> … chemical or electrical induction of parthenogenesis is a frequently utilized research tool to initiate development without fertilization for the study of oocyte developmental competence.
> *Associate Professor Jeremy Thompson, Deputy Director, Research Centre for Reproductive Health, University of Adelaide (Confidential submission LRC266; reproduced with permission of the author)*

However, parthenogenetic activation of oocytes, when oocytes are activated to start embryonic development without fertilisation with a sperm, is also illegal under the PHC Act and therefore this test is also not available to researchers. Further discussion of parthenogenesis and other anomalies relating to activation and fertilisation is included below.

Interspecies fertilisation

Research for the improvement of ART practice using experimental fertilisation has been further inhibited by the prohibition on creation of hybrid embryos. For example, ART researchers and practitioners were previously able to undertake fertilisation studies using human sperm and animal oocytes (eg hamster) to test sperm quality. This is no longer possible under the RIHE Act.

Sydney IVF (Submission LRC819) argued that the prohibition in such cases should be on the placement of a hybrid embryo in a woman's uterus, rather than on the creation of such an embryo.

Embryology studies

Some ART researchers indicated that a number of valuable studies could be done if it were possible to use embryos created from eggs and sperm specifically for research up to the stage of implantation. This is prohibited by the current legislation.

Sydney IVF commented that basic embryology researchers could use donated gametes to create embryos. Sydney IVF also indicated that access to fresh fertilised embryos is required for research that would protect ART consumers from potential problems with new treatments. If this research is prevented, recipients of clinical ART treatments become de facto 'guinea pigs' in the development of the technologies:

> If fertilization procedures may not be examined for safety by destructive analysis of embryos up to the stage of implantation, the end-point for the investigation of the safety of new IVF procedures or variants of established IVF procedures becomes the normality or otherwise of babies born. *Sydney IVF (Submission LRC819)*

In this connection (technology moving into clinical practice before it has been fully evaluated), Associate Professor Jeremy Thomson told the Committee that this had occurred overseas for IVM of oocytes:

> Therefore, research into *in vitro* maturation to improve the efficiency is essential, as although the technique is slowly being taken up clinically, several hundred babies have now been born worldwide through the use of IVM. *Associate Professor Jeremy Thompson, Deputy Director, Research Centre for Reproductive Health, University of Adelaide (Confidential submission LRC266; reproduced with permission of the author)*

Since the legislation was passed, frozen excess ART embryos have been used under licence in some embryology studies, such as testing of culture media. However, Sydney IVF cautioned that:

> Research involving excess embryos alone cannot answer research questions that centre on fertilisation and the in vitro preparation of eggs for fertilisation. *Sydney IVF (Submission LRC819)*

The current legislation also prohibits the use of fresh excess ART embryos through the consent process. The 14-day cooling-off period that is required after embryo donors give consent for a specific research project but before the embryo is used (see Sections 11.1 and 11.2) limits the use of fresh embryos:

> We seek further clarification on the status of such embryos [abnormally fertilised embryos, ie created by IVF] and request consideration be given to developing a prospective consent process that would allow the use of such fresh embryos for potential research and training. *IVF Australia (Submission LRC346)*

Professor HW Gordon Baker also stated that modifying the legislation to maximise research on excess ART embryos would be helpful, if fertilisation studies and the formation of cleavage stage embryos were to remain banned. Under previous Victorian legislation, discarded embryos that had been left to succumb for 24 hours were available for research. Professor Baker told the Committee that, if discarded embryos were cultured and histologically fixed, studies such as embryo metabolism, protein distribution and cell counts might be possible:

> Such studies might have some utility for testing new culture medium additives or developing tests on embryonic metabolites in the medium that might predict the quality of the embryo and its chances of producing a continuing normal pregnancy.
> *Professor HW Gordon Baker, Victoria (Supplementary submission LRC391)*

Finally, Sydney IVF suggested that some research using chimeric embryos should be allowed, because the harm comes from implanting a prohibited embryo into the uterus of a woman, rather than from simply producing the prohibited embryo. Sydney IVF recommended that the Committee:

> Reconsider the need for s20, perhaps requiring approval at a national level (eg by AHEC or the minister) for potentially insightful research in the area of chimaerism [sic], a natural process. *Sydney IVF (Submission LRC819)*

See Section 7.2 for further discussion of creation of embryos by fertilisation for research.

Cytoplasmic transfer

Cytoplasmic transfer has been used as a fertility treatment overseas (see Section 4.2 of the literature review). However, by 2001 concerns had been raised about the safety of the procedure and it ceased in ART clinics pending further research. This method was particularly used for older women, whose eggs can no longer produce a viable embryo. The method is also being investigated overseas for prevention of mitochondrial diseases, which are currently untreatable diseases caused by metabolic failure of cells.

However, research on cytoplasmic transfer has been prohibited in Australia under the PHC Act since 2002 because it would result in an embryo containing genetic material from more than two people. Sydney IVF submitted:

> … the intent of these sections [PHC Act ss15,18] is to prevent egg cytoplasm (the fleshy, non-nuclear part of the egg) being transfused from a donated egg to an egg deficient in its own cytoplasmic metabolism — on the trivial grounds that it contains a small amount of mitochondrial DNA … Without the option of cytoplasmic transfer, families affected by mutations of mitochondrial DNA, such as the mitochondrial form of Leigh's disease cannot now be helped in Australia to have disease-free children. *Sydney IVF (Submission LRC819)*

The submission from the Queensland Government suggested that further research on cytoplasmic transfer would be necessary to establish the safety of the technique, but that such research is currently prohibited:

> Under the current Australian legislation, cytoplasmic transfer is prohibited as it would result in the creation of an embryo with genetic material from more than two people. However, it is worth noting the technique. If efficacy and safety can be proven, and the role of third party mitochondrial DNA identified, the technique may have the potential to become an acceptable tool in ART. With the current prohibition, Australian scientists will not be able to participate in research to determine the safety of the practice for ART purposes and ART practitioners will not be able to utilise the technique for ART procedures.
> *Queensland Government (Submission LRC930)*

Sydney IVF, and others, further noted that the added mitochondrial DNA is not expressed in the child except for the fact that normal cellular metabolism is restored. Sydney IVF adds:

> Women wishing to have a baby must accept donated whole eggs and thus have a child that is genetically not their own but that of the donor, whereas using just the cytoplasm of a donated egg would mean that they can truly have their own child, an aim that is unjust to render illegal. *Sydney IVF (Submission LRC819)*

Alternative methods of producing gametes

As animal studies have indicated it is possible to create gametes from embryonic stem cells (see Section 4.2), ART researchers are clearly interested in investigating the use of this method in humans to create eggs or sperm for people who do not produce their own (Submission LRC346).

This technique and other novel methods of producing gametes are being developed overseas (see Section 4.2) but cannot be developed for human use in Australia under current legislation.

Use of parthenogenetic activated oocytes and other 'abnormally fertilised embryos'

Although the Explanatory Memoranda to the Acts (see Section 2.1) refer to parthenogenetic activation by mechanical or chemical stimulation of human eggs, several researchers told the Committee that this type of activation occurs in nature and also as a spontaneous process in IVF laboratories:

> The process of parthenogenesis can be a naturally occurring event, especially in IVF laboratories by accident. 'Aged' mature oocytes appear to be more sensitive to parthenogenetic stimuli (which can include environmental stresses), which in many ways is akin to the depolarization events associated with nerve signal transduction. It is known to occur in vivo as well. *Associate Professor Jeremy Thompson, Deputy Director, Research Centre for Reproductive Health, University of Adelaide (Confidential submission LRC266; reproduced with permission of the author)*

Researchers indicated that parthenogenetically activated oocytes and other 'abnormally fertilised embryos' (that would otherwise be discarded) would be useful for other potential research and training purposes, including the extraction of stem cells. IVF Australia indicated that a range of 'abnormally fertilised embryos' occur in IVF laboratories and are discarded. The centre said that such embryos do not have a normal chromosome component and are only capable of limited development, and suggested that abnormally fertilised embryos could be used for research or made available to IVF laboratories for training embryologists in techniques such as PGD (Submission LRC346).

At the Adelaide hearings, Dr Peter Woolcock, representing the South Australian Council on Reproductive Technology (SACRT) said that members of SACRT are mainly involved in ART research rather than stem cell research. Some think that it would be useful to be allowed to use parthenogenetic embryos (activated oocytes), because this would allow researchers to investigate what turns genes on and off and what makes embryos develop; however, SACRT does not have a formal position on oocyte activation.

In its submission, Sydney IVF also referred to important research on oocyte tumours (teratomas), which are the most common oocyte tumours in women. The centre commented that this research has been hampered because of the legislation banning the creation of parthenogenetically activated oocytes:

> Research into the causes of the commonest ovarian tumour found in Australian women, tumours of the oocytes (eggs) known as teratomas, or 'dermoid cysts', is now potentially a felony. *Sydney IVF (Submission LRC819)*

> I just say this as a personal comment and certainly not one of the Fertility Society. We see this occasionally that if oocytes we've collected before they're inseminated have been parthenogenically activated they develop two [pronuclei] — they divide … We treat them as any other abnormally fertilised egg and discard them.
> *Dr Keith Harrison, Scientific Director, Queensland Fertility Group (Brisbane hearings)*

Thus, these respondents argued that this type of spontaneous parthenogenesis should not be illegal. Further, a number of scientists who spoke to the Committee argued that parthenogenetically activated oocytes do not have the potential for human development past a very early stage of development and therefore should not be regarded as embryos. Some community respondents agreed that if the development of activated oocytes did not parallel human embryo development, then they should not be regarded as embryos.

At the Sydney hearings, the Most Reverend Professor Anthony Fisher, Auxiliary Bishop to the Most Reverend Dr George Pell, Archbishop, Catholic Archdiocese of Sydney, said that if a human organism can progress to the later stages of human development, it should be treated as an embryo. However, if it follows a developmental path that does not parallel human embryonic development in any way, then it could be regarded as similar to other tissues. In general, he agreed that if a cell is totipotent, it would be regarded as a human embryo.

The literature review reported that mammalian oocytes can be stimulated to undergo parthenogenesis in vitro by using chemical methods that mimic the action of sperm. While mouse parthenotes can develop past implantation, primate parthenotes can only reach implantation. This arrest in development is because all the genetic material comes from the mother, so there is no paternal imprinting, which is

thought to be responsible for the development of the trophectoderm and primitive endoderm. However, as primate parthenotes can develop to the blastocyst stage, this process has been used to derive primate stem cells.

Requirements for nuclear reprogramming for parthenogenesis and for somatic cell nuclear transfer are closely related. The mechanism of nuclear transfer is also becoming much better understood, as has been shown lately by the successful creation of both human and other primate nuclear transfer embryos. Therefore, the possibility of applying similar reprogramming techniques to the activation of oocytes, thus creating parthenogenetic embryos with the potential for development to a full organism, cannot be completely ruled out.

Training and quality assurance activities

IVF providers and researchers commented on the impact of the legislation on embryology training and quality assurance.

At the Brisbane hearings, Dr Keith Harrison, Scientific Director, Queensland Fertility Group, told the Committee that, although new embryologists are trained in manipulation techniques using mouse embryos, training in embryo biopsies requires human embryos. He noted that the legislation had made it more difficult to train embryologists in techniques such as PGD, and had affected quality control:

> PGD is a low throughput service. It's sufficient only to maintain the expertise of a couple of operators … It's impractical for us to provide ahead of time a trainee embryologist's name and the number of embryos required to the Licensing Committee because we can't predict who we'll have to train until that happens, and we also can't predict the number of embryos that are going to be required. And we also can't tell how many embryos we'll need to determine a quality control issue. So these requirements have resulted in the fact that we just don't use these embryos for this purpose. However, it would benefit our practice and our patients' outcomes if we could more easily use them for this purpose. *Dr Keith Harrison, Scientific Director, Queensland Infertility Group (Brisbane hearings)*

To avoid this problem, Dr Harrison suggested either making quality control issues and embryologist training exempt from the research guidelines, or granting clinics blanket licences for embryology training with reporting and external audit requirements (see Chapter 8). Alternatively, some ART practitioners suggested that abnormally fertilised embryos and other embryos not suitable for implantation should be made available for research and training.

(See 'Use of parthenogenetically activated oocytes and other 'abnormally fertilised embryos', above, for a discussion of the use of nonviable embryos for training.)

Use of embryonic stem cells for ART research

Some ART researchers told the Committee that, in the future, embryonic stem (ES) cell lines (such as those that may be obtained from a stem cell bank) would be useful tools for ART research as they may provide good metabolic models of embryos. For example, it may be possible to test culture media and do quality assurance assessments using ES cells instead of embryos themselves. Furthermore, research on frozen storage has been done using stem cells in an attempt to refine freezing protocols (Submission LRC346).

Use of excess ART embryos created after 5 April 2002

The RIHE Act, section 24(3), stated that licences for destructive research using excess ART embryos were restricted to embryos created before 5 April 2002. This clause was included because of concerns that, if research were permitted on excess ART embryos, ART clinics might create more embryos than needed for ART treatment to ensure an ongoing supply of excess embryos for research.

The Act included a further clause at section 46 that repealed section 24(3) on 5 April 2005. Thus, since 5 April 2005, researchers have had access to all excess ART embryos, irrespective of when they were created.

Researchers felt that the lifting of this restriction was beneficial:

> Removal of the clause limiting donation of embryos frozen before 5th April 2002 was extremely beneficial to researchers and patients wishing to donate excess embryos. A broader range of options now exist for people to choose what to do if they are in a position to have excess embryos following fertility treatment.
> *Fertility Society of Australia and Monash IVF (Submission LRC218)*

This was also the position of the Victorian Government:

> With safeguards to reassure the community that research is conducted in an ethical manner the Victorian government submits that there be no reintroduction of restriction of access to surplus assisted reproductive technology embryos created at any particular date.
> *The Hon John Brumby, Victorian Treasurer and Minister for Innovation (Melbourne hearings)*

Others also supported the lifting of the restriction and stressed that there was no need to have a new sunset clause in any revised legislation:

> Given that the Australian Government has established a rigorous regulatory regime involving NHMRC licenses, Victoria believes there is little point in re-introducing a restriction on access to surplus ART embryos created at any particular date.
> *Government of Victoria (Submission LRC537)*

4.4 Summary — developments in ART

It is clear that areas of ART research have been impeded or stopped altogether since the PHC Act and the RIHE Act were introduced. This is because:

- the legislation prohibits the creation of human embryos for research
- human embryos are defined as starting from the appearance of two pronuclei
- the creation of parthenogenetic embryos is prohibited
- the creation of hybrid embryos is prohibited
- the creation of embryos with genetic material from more than two persons is prohibited.

These conditions rule out any experimental fertilisation, oocyte activation or developmental embryology research. In addition, the use of fresh, excess embryos from ART programs, including those not fit for implantation, is precluded because of the consent process and unclear definition of an excess ART embryo, thus also ruling out the use of these embryos in ART research. Finally, the licensing requirements place a significant barrier on training and quality assurance activities, further limiting the progress and quality of developments in ART.

5 Developments in medical and scientific research: stem cell research

5.1 Background to stem cell sciences

Stem cells have been of great interest to researchers for several decades because of their potential to regenerate damaged or diseased tissues. They also provide a good model for research on the development and function of different cell types, the features of diseases at a cellular level, and the effects of chemicals and drugs on different cell types.

Stem cells differ in their potential to generate different cell types, as follows:

- *Totipotent stem cells* are cells from the very early stages of embryo development, after fertilisation, which can, if separated, develop into a whole organism (ie cells that can give rise to all tissues and cell types of the developing organism, including the placenta and other supporting tissues).
- *Pluripotent stem cells* are cells that can give rise to all or many cell types of the body from all three primary layers (ectoderm, mesoderm and endoderm) but not to a whole organism.
- *Multipotent stem cells* are cells that can give rise to a few different cell types, such as the blood-forming cells in bone marrow, which form all the different types of blood cells.
- *Unipotent stem cells* are cells that only give rise to one cell type (such as skin or cornea).

Sources of stem cells

While unipotent and multipotent stem cells may be useful for tissue repair, an important goal of stem cell researchers has been the isolation, characterisation and culture of pluripotent stem cells. Pluripotent cell lines have indefinite self-renewal capacity in culture while remaining in an undifferentiated form. However, with the right stimuli, these cells can differentiate into many cell types. This potential ability to generate healthy cells of different tissue types (liver, kidney, nervous tissue) in a laboratory has been the stimulus for the highly active area of medical research called ‘regenerative medicine’, to repair damaged or defective cells and tissues in the body.

At the earliest stage of development after conception, each cell is totipotent (which is the basis for embryo splitting, or ‘twinning’). After a few days, however, the cells form a fluid-filled sphere called the blastocyst. From this stage onwards, individual cells do not have the capacity to develop into a whole organism. The cells in the outer layer of the blastocyst give rise to the placenta and other supporting tissues. The cells in the centre (the inner cell mass) give rise to the developing body layers (endoderm, mesoderm and ectoderm) of the developing embryo and fetus, and ultimately to all the organs and tissues of the body (approximately 210 different cell types). The cells of the inner cell mass can be extracted from the blastocyst and cultured to derive so-called ‘embryonic stem cells’ (ES cells), which are considered by many researchers to be the most flexible source of pluripotent cells.

In animals, the primordial germ cells (ie the cells in the embryo that will develop into gametes), which are obtained from embryos after implantation, have also been found to be a good source of pluripotent stem cells. These cells are called ‘embryonic germ cells’ (EG cells). Similar pluripotent stem cells also occur in fetuses and the blood from the umbilical cords of newborn babies.

ES cells and EG cells were first obtained from mouse embryos and cultured in the laboratory in the early 1980s. This was followed by an explosion of work on retrieval and culture methods for mouse embryonic cells. ES cells can be cultured in the laboratory and expanded to very large numbers (one flask of cells can be expanded to several hundred flasks in a matter of weeks, with each flask containing several million cells). The pluripotent potential of mouse ES cells was confirmed by

injection of the cells into a mouse blastocyst and demonstration that they gave rise to all cell types. It was not until 1998, however, that the first culture of human ES cells was achieved (reviewed by Pera and Trounson 2004).

After birth, most tissues and organs have some stem cells. For example, the lower layers of skin have stem cells that generate new skin as old skin is lost, similar cells in the gut regenerate the lining of the intestines, cells in bone marrow generate new blood cells as old ones are lost, and so on. Stem cells obtained after birth (including cord blood cells) are collectively referred to as 'adult stem cells' (AS cells) and have a variable potency (ie potential for differentiation into different cell types). AS cells have been cultured and used to research and develop cellular therapies in the same way as for ES cells.

Challenges for stem cell research

There are several challenges for stem cell researchers in the development of cellular therapies. These include:

- maintaining stem cell lines in culture without them becoming degraded
- controlling differentiation to derive populations of the required cells
- ensuring that transplanted cells assume the required structure and function, and do not develop into tumours or cause other unwanted side effects.

In addition, to be used successfully in cellular treatments, stem cells must withstand the immune barriers to transplantation (as for organ transplants). ES cell researchers believe that this can be done by creating embryo clones of the person to be treated and extracting the patient-matched ES cells (so-called 'therapeutic cloning'). AS cell researchers believe it will be possible to obtain cells from the person requiring treatment, thus also overcoming the rejection problem.

In 2001, there was no agreement among researchers about whether adult or embryonic stem cell research was likely to be most successful; however, most considered that all avenues of research should be pursued until the outcomes become clearer. (See Bongso and Richards 2004 for an overview of stem cell research.)

Review findings

The remainder of this chapter summarises the findings of the literature review referred by the Minister of Ageing for stem cell research since 2001 (Biotext 2005; see Section 3.3) and the other information received by the Committee during the reviews. The focus of the chapter is on stem cell research in general terms — that is, the establishment and culture of the cells to establish and maintain cell lines; the generation of specialised cells for studies of cell development and disease processes; and development of potential cellular therapies. Further information on cloning and the creation of patient-specific stem cells extracted from human embryo clones (so-called 'therapeutic cloning) is included in Chapter 6.

5.2 Literature review – advances in stem cell sciences since 2001

Research on the growth and differentiation of stem cells for scientific investigations, development of cellular therapies and investigation of disease development has increased rapidly since 2001. Most work has focused on rodent, nonhuman primate and human embryonic and adult stem cells. This is an extremely active area of research, and the literature review was only able to provide an overview of the most general reviews covering the main issues relating to embryonic and adult cell types. Further details from the literature review, including methods, results of the searches and all relevant scientific references, can be seen on the Legislation Review website.[18]

Embryonic stem cells

By 2001–02, research in human ES cell biology was widespread in Australia, Europe and the United States, with other significant research teams also in Israel and Singapore. Cell lines were being developed and distributed in the United States to assist research. At that time, cardiomyocytes and neural cells derived from ES cells had been successfully transplanted into animal models. Nerve cells derived from EG cells in mice had partially restored spinal function in rats, and there had been some early clinical trials of stem cell therapy for stroke and other conditions.

ES cell lines have now also been developed from several species of nonhuman primates; by 2004, there were 18 rhesus monkey ES cell lines and four cynomolgus macaque monkey ES cell lines. However, contamination and spontaneous differentiation into different phenotypes are common problems for nonhuman primate ES cell lines. (See Keller 2005 for an overview of ES cell research.)

Culture conditions

To provide suitable conditions to grow undifferentiated stem cells, early cultures used animal feeder cell layers (usually irradiated mouse cells) and growth media containing animal serum. The debate in the early 2000s about the potential for infectious disease transmission from animals to humans as a result of transplanted animal tissues and cells (xenotransplantation) highlighted the need to develop culture methods for human stem cells that are free from animal products. To date, most stem cell types, including human ES cells, cannot be grown efficiently in serum-free conditions. Using growth factors to develop culture conditions to improve growth in serum-free conditions is therefore the focus of much current research.

Differentiation

In early research with stem cells, the cells were injected into animal models at the disease or injury site of interest (eg brain, heart), and differentiation was allowed to proceed in vivo. However, undifferentiated cells have the potential to form mixed-cell tumours called teratomas and it is now recognised that, to minimise the risk of teratoma development, stem cells need to be fully differentiated before transplantation.

Recent research has harnessed the increased knowledge of growth and transcription factors, as well as modern genetic manipulation technology, to develop protocols for in vitro differentiation of ES cells. Differentiation mechanisms are not fully understood for any cell type, and therefore this work is still at an early stage of development. Nevertheless, neurones, cardiomyocytes, endothelial cells, smooth muscle cells, haematopoietic cells, osteogenic and epidermis cells, hepatocytes and insulin-producing cells have all been differentiated from human ES cells in culture.

(For information on culture and differentiation of ES cells, see Gerecht-Nir et al 2003, Carpenter et al 2003, Bongso and Richards 2004, Gerecht-Nir and Itskovitz-Eldor 2004, Heng et al 2004, Pera and Trounson 2004, Shufaro and Reubinoff 2004, Keller 2005.)

Adult stem cells

Plasticity of adult stem cells

Following the characterisation of a number of AS cells, the possibility was raised that the differentiation of some of these cells could be redirected away from their ‘home’ tissue (such as bone marrow, skin or brain). This ability to transdifferentiate has been called ‘plasticity’. In 2001 it was suggested that some AS cells may show higher levels of plasticity than originally thought, making

18. See http://www.lockhartreview.com.au

them potentially pluripotent. Although subsequent studies have demonstrated that some adult cells are more flexible than had been previously thought, the mechanisms controlling these processes remain poorly understood.

AS cells that have shown substantial plasticity are:

- haematopoietic stem cells — found in bone marrow, spleen, fetal liver and umbilical cord blood; capable of forming all blood cell types as well as a variety of other cell types, including skin, cardiac and skeletal myoblasts, liver cells, bone and neural cells
- bone marrow stromal (BMS) cells (also called mesenchymal stem cells) — found in bone marrow but distinct from haematopoietic cells; capable of forming various connective tissue cell types (including bone, fat, tendons and stromal cells) as well as liver, lung, gut, cardiac and skeletal muscle and neural cells
- neural stem cells — found in brain tissue (but also accessible through the olfactory system of the nose); capable of forming all types of nervous tissues as well as haematopoietic elements.

The extensive research in this area since 2001 has provided a complex and sometimes controversial picture of the plasticity of AS cells, and of whether any AS cell types can be truly regarded as pluripotent. Some research has indicated that transdifferentiation may occur as a result of other cellular mechanisms, such as cell fusion (Raff 2003, Grove et al 2004, Rodic et al 2004, Wagers and Weissman 2004). To resolve these issues, mechanisms of transdifferentiation are the subject of intense ongoing research and review.

Isolation and culture

AS cells are dispersed through different tissues of a mature organism at different frequencies and states of activity. The isolation and purification of these cells are therefore difficult, and no specific markers of AS cells have been defined. Even the most purified bone marrow stem cells are highly heterogeneous.

Once isolated, AS cells can be cultured using methods similar to those used for ES cells, and many cell lines have been developed (reviewed by Heng et al 2004). As for ES cells, serum-free culture conditions have been developed for AS cells, but the cells do not grow as well in these conditions as they do in the presence of serum. Therefore, researchers are using various combinations of growth factors to promote better proliferation and differentiation (Heng et al 2004).

Development of disease therapies using stem cells

The development of cellular therapies using adult and embryonic stem cells is an extremely active area of research covering a wide range of diseases, conditions and injuries. New information emerges daily, and many cell types and procedures show potential in animal studies. The focus of the literature review was on new applications and developments in stem cell therapies since 2001, rather than on previously established techniques, such as bone marrow transplantation.

Many preclinical studies have been reported in the literature, using different experimental and animal models, cell types and conditions. The review, therefore, presented only a very broad overview of these studies. Clinical trials have ranged from case reports on individual patients to larger randomised controlled trials (RCTs). Some potential therapies have reached phase 1 and 2 clinical trials (eg heart cells, neural cells). Since 2001, most of these trials have involved AS cells because, at this stage, ES cell research has not reached the stage needed to start clinical trials (ie proof of principle of a safe and efficacious treatment in animal models).

The variety of potential sources for AS cells and increasing evidence of their plasticity is providing many new opportunities for research into potential therapies using these cells. However, most AS cell populations are highly heterogeneous, so the derivation of well-characterised differentiated cells for transplantation presents challenges similar to those for ES cells. This means that significant preclinical and clinical development is required before safe, effective therapies become available.

Table 5.1 summarises preclinical and clinical research for some of the major diseases/conditions and injuries discussed in the media in association with stem cell research. Further details are included in Chapter 7 of the literature review.

Growing cell lines to study disease progress in vitro

Since 2001, there has been increasing interest in the use of stem cells as models to study the development of disease. Some stem cell lines have been developed that mimic certain disease states. Several neurodegenerative diseases, including Alzheimer's disease, have been induced in mouse embryos by microinjecting DNA into the embryo. ES cell lines from these embryos can be used to study the cellular physiology of the disease (Shaughnessy et al 2004).

In February 2005, researchers in the United Kingdom started a project to take cells from patients with motor neurone disease and create cloned embryos, which will produce stem cells for study of the disease.[19]

Drug testing

Human ES cell-based in vitro screening models are being developed for testing the chemical toxicity and pharmacological action of chemical agents. Such systems have not yet been widely used or tested, but further development may allow researchers to test drugs and potential chemical toxins without the use of animals (see Gorba and Allsopp 2003 for review).

19. See http://www.hfea.gov.uk/PressOffice/Archive/1107861560

Table 5.1 Summary of preclinical (animal) studies and clinical trials with stem cells for some major diseases featured in the media

Condition	Preclinical studies	Clinical trials
Heart disease	**Embryonic stem cells** — differentiation to cardiomyocytes, transplantation and improved cardiac function in several animal models. **Adult stem cell**s — transplantation of allogeneic or autologous fetal, neonatal and adult cardiomyocytes, skeletal myoblasts and smooth muscle cells have all led to improved cardiac function in animal models. Injection of bone marrow stromal (BMS) cells has improved cardiac function, and combinations of cells are also being investigated.	There have been several phase 1 or 2 trials with autologous adult stem cell (AS cell) populations, with improvements in cardiac function. There have not been any large randomised double-blinded trials.
Diabetes (type 1)	**Embryonic stem cells** — differentiation to insulin-forming cells; transplantation and control of hyperglycaemia in animal models. **Adult stem cell**s — differentiation of various AS cells to insulin-forming cells; transplantation and control of hyperglycaemia in mice.	Small trials before 2001 using fetal tissue. Reduced insulin requirement but did not reverse diabetes. None since 2001.
Spinal cord injury	**Embryonic stem cells** — transplantation of mouse ES cells led to differentiation in vivo with improved function in rats, but teratomas formed. Mouse ES cells differentiated in vitro also improved function when transplanted. **Adult stem cell**s — BMS cells transplanted and improved function in rats; olfactory sheathing cells (not stem cells as such) have promoted significant recovery of motor and sensory functions in rat models.	Several phase 1 trials have shown feasibility of AS cell transplants. Functional improvements inconclusive. Some further trials in progress with olfactory sheathing cells
Stroke	Transplantation of ES and AS cells (including BMS cells) in animal models has led to partial improvement in behaviour, with cells proliferating and differentiating into neural cell types.	Phase 1 study in 2000 (n = 12, no controls) of neurone cultures — some improvements. Randomised control trial in the Republic of Korea of bone marrow mesenchymal cells (AS cells) — some evidence of improvement.
Parkinson's disease	**Embryonic stem cells** — differentiation to dopaminergic neurones and transplantation in mice/rats led to improved function. **Adult stem cell**s — differentiation of various AS cell types to dopaminergic neurones and transplantation in mice/rats led to increased dopamine production.	Various small trials (mainly fetal cells) — inconclusive results and some serious adverse effects (dyskinesia). A phase 2 trial is in progress in the United States with cultured retinal pigment epithelial cells (68 patients).
Huntington's disease	AS cell, ES cell and cord blood-derived neural cells transplanted in rat Huntington's disease models. Developed neurones with some improved health outcomes.	Numerous small safety trials using fetal brain cells. Clinical benefit reported.

5.3 Submissions and hearings on stem cell science

Licensed research relating to stem cell extraction

Since the Licensing Committee was appointed in 2003, four applications have been received and four licences granted for research to derive human ES cell lines. Details of these licences are shown in Table 5.2.

Table 5.2 Licences issued for research on extraction of embryonic stem cells

Organisation	Licence no.	No. of embryos	Licence title	Dates
Sydney IVF Pty Ltd	309703	50[a]	Development of human embryonic stem (ES) cells	16/4/04 – 16/4/07
Melbourne IVF Pty Ltd	309709	200[b]	A collaborative project between Melbourne IVF Pty Ltd and Stem Cell Sciences Pty Ltd to derive human embryonic stem cell lines	11/6/04 – 11/6/06
IVF Australia Pty Ltd	309708	100[c]	A collaborative project between IVF Australia and the Diabetes Transplant Unit, Prince of Wales Hospital, to derive human embryonic stem cell lines for the treatment of diabetes	5/11/04 – 5/11/07
Monash University	309707	200[d]	Derivation of embryonic stem cell lines from the human embryo	21/12/04 – 21/12/07

a 35 must have been used first under licence 309701. In addition, inner cell masses of embryos used under licences 39702A and 30702B can also be used to derive stem cells under this licence.

b This is the maximum number that can be removed from storage. The licence allows derivation of six human ES cell lines (ie once six cell lines have been derived, no further embryos may be thawed).

c This is the maximum number that can be removed from storage. The licence allows derivation of six human ES cell lines (ie once six cell lines have been derived, no further embryos may be thawed).

d This is the maximum number that can be removed from storage. The licence allows derivation of 20 human ES cell lines (ie once 20 cell lines have been derived, no further embryos may be thawed).

Source: Database of licences authorising the use of excess ART embryos, NHMRC (http://www.nhmrc.gov.au/embryos/monitor/database/index.htm)

Sydney IVF reported that, under Licence 309703, it derived Australia's first ES cell line. The submission also stated that the success rate for producing a stem cell line from a clinically usable embryo at Sydney IVF is about 50%. Furthermore, the submission highlighted the fact that each stem cell line could be a tissue match for the children of the couple who produced the embryo:

> Each stem cell line has more than a one-in-five chance of being a perfect tissue match for any child of the couple who produced the embryos. Whatever the research or commercial or therapeutic purpose the stem cell lines are put to, it is a relatively simple matter to reserve a small aliquot of early stem cells for future access to the family donating the particular embryo or embryos. *Sydney IVF (Submission LRC819)*

Stem Cell Sciences Ltd (Submission LRC318) reported on its collaborative project with Melbourne IVF and the Australian Stem Cell Centre, under Licence 309709. Researchers in this program are in the final stages of producing the first two fully characterised lines available for distribution by the Australian Stem Cell Centre (MEL 1 and MEL 2). These two cell lines will also be accepted by the UK Stem Cell Bank (and therefore made widely available to international researchers). Stem Cell Sciences Ltd told the Committee that these are the first two cell lines of six intended lines in the MEL series. All six MEL lines will be made available to Australian and international researchers and companies.

A major research interest for Stem Cell Sciences Ltd and other researchers in this field is to understand how to sustain stem cells in a primitive, undifferentiated state, which is essential for large-scale expansion of human ES cells:

> In addition to the research exploring the differentiation potential of human embryonic stem cells, a major interest of many research groups is to better understand how to sustain stem cells in a primitive, undifferentiated state. The ability to maintain the cells in culture is essential for large scale expansion of human embryonic stem cells.
> *Stem Cell Sciences Ltd (Submission LRC318)*

The Diabetes Transplant Unit (DTU), Prince of Wales Hospital, Sydney (Submission LRC180) (working in conjunction with IVF Australia under Licence 309708), reported that it has produced one human ES cell line. Researchers in DTU are able to differentiate human and mouse ES cells into insulin-producing cells, but need to optimise this process if the cells are ever likely to be of therapeutic benefit. DTU also reported that it would like to facilitate the use of human ES cells for medical research in areas other than diabetes treatment, such as neurones for treatment of spinal cord injuries; limbal and retinal cells for the treatment of blindness; liver cells as a therapy for chronic liver failure; and eggs for treatment of infertility. In addition, the unit indicated that ES cells could also be used in a range of other research activities, including examination of the effect of viruses on human tissue, proteomics, comparison of stem cells from different sources (eg cord blood and placenta), and developmental biology (eg methylation of genes, biochemistry of developing ES cells).

In expectation of the clinical usefulness of ES cells, DTU is also in the process of establishing a facility at the Prince of Wales Hospital in which human ES cells can be produced and maintained under ‘good manufacturing practice’ conditions. Such conditions will be required by the Therapeutic Goods Administration before cells can be used in humans.

A Monash University research team headed by Dr Martin Pera, Professor Alan Trounson and others and funded by the Australian Stem Cell Centre (ASCC) is working under the most recently awarded licence (Licence 309707) for deriving new ES cell lines for further research on defined culture conditions. The project is linked to the International Stem Cell Initiative (Dr Pera is a member of the steering group), which is coordinating the analysis of large numbers of human ES cell lines:

> We do not yet know with any certainty, for instance, if certain hESC lines are superior at forming certain types of tissue cells, or if certain methods of propagation enhance the yield of stem cells with particular desired characteristics. These are major imperatives underpinning future regenerative medicine initiatives worldwide. In summary, there is still a strong case for ongoing efforts to derive new stem cell lines, particularly since this is a rapidly developing field in which technical innovation will result in steady improvement in the means for producing and maintaining hESC. *Monash University (Submission LRC509)*

ASCC was established three years ago as a partnership between the Australian Government, the scientific community and academia. Professor Stephen Livesey, Chief Scientific Officer of ASCC, is co-director of the International Consortium of Stem Cell Networks. The Victorian Government recently announced a two-year funding grant to ASCC to establish a secretariat for the International Consortium at the centre’s office in Melbourne. The International Consortium was set up in 2004 after a meeting of national stem cell centre representatives. It is a complementary vehicle of the International Stem Cell Forum, which was established in 2003 to bring together funding agencies for stem cell research (including the NHMRC).

Further information on international exchange of ES cells and research collaboration is in Chapter 13 and Chapter 15.

Opposition to ES cell research

There were numerous submissions and hearing transcripts that stated opposition to ES cell research. Many of these respondents proposed an increase in funding for AS research and reduced funding of ES cell research, stating that AS cell research was as good as ES cell research, if not better. The following extracts are typical of many of these submissions:

> the evidence indicates that embryo stem cell research … has been a choice for a science which is not ethical … and … is winning funding disproportionate to its promises and in a way that wastes time and money that could be going towards science which is ethical and is paying real dividends in human health today, i.e. adult stem cell research …
> *Christian Adult Social Institute Inc (Submission LRC406)*

> … to date in Australia, access to excess ART embryos for research has not led to a significant advance in knowledge in the areas of stem cell science and cell therapy research.
> *Australian Catholic Bishops Conference (Submission LRC481)*

> With a limited number of research dollars to fund work, we cannot afford, and it is not acceptable, to take money away from the research that is getting results right now.
> *Mrs Alice Fiumara, New South Wales (Submission LRC132)*

The reasons for lack of support for ES cell research and support of AS research were varied. Some said that, as some human ES cell lines have now been created and are now available for research, there is no reason to create further ES cell lines:

> The issuing of licenses for the creation of new stem cell line is unwarranted as there are already sufficient stem cell lines in existence to do all the basic research. This research has not yet established that human embryonic stem cells will ever be able to be used safely and effectively for therapies. *National Civic Council (Submission LRC246)*

Other respondents focused on safety issues associated with using ES cells, including the risk of tumour (teratoma) formation after transplantation, and immune rejection of the cells:

> … the lack of the use of embryonic stem cells in clinical trials illustrates the continuing problems associated with embryonic stem cells including immune rejection and uncontrolled growth. *Professor Alan Mackay-Sim, Eskitis Institute of Cell and Molecular Therapies, Griffith University (Submission LRC217)*

> There are serious and possibly insurmountable biological problems with embryonic stem cells. These are the problems of rejection where the stem cells are recognised as ‘foreign’ and destroyed, or unmodulated growth leading to malignancy when they do survive.
> *Dr David M Gawler, Northern Territory (Submission LRC319)*

Many submissions were also doubtful of the therapeutic potential of ES cells, often contrasting this with examples of successes with AS cells:

> Nothing in the experiments on human cloning in Britain or Korea have improved the likelihood that this will ever lead to successful therapies. There is still not a single therapy utilising human embryonic stem cells, whether from a cloned human embryo or an embryo created by IVF.
> *National Civic Council (Submission LRC246)*

> To date, there have been no successes with embryonic stem cells for the treatment of any medical condition … Adult stem cell technology has by contrast been a great success.
> *Mr John Hart, Victoria (Submission LRC156)*

However, although the stated reasons for lack of support for ES cell research were that it had not shown results or had less potential for success than AS cell research, it was clear that the main objection to ES cell research is because of ethical concerns about the destruction of human embryos (see Chapter 7).

Objections to human ES cell research were not confined to the nonscientific community. Recent remarks by British infertility specialist and science broadcaster, Professor Lord Robert Winston, criticising the 'hype' that has surrounded discussion of ES cell research, were cited by several respondents.

Some Australian scientists also spoke against any loosening of the current restrictions on destructive embryo research. At the Melbourne hearings, Emeritus Professor Jack Martin, University of Melbourne, argued that the current prohibitions and regulatory arrangements are in place because of the ethical objection to destroying human embryos (a position that he holds). In his written submission, he told the Committee that he believes that lifting ethical barriers could be considered if, and only if, animal models show clear proof of concept, and the potential for clinical trials and human benefits exists:

> For several of these conditions there are appropriate experimental models that can be studied in animals, but in no case have embryonic stem cells been shown in animal research to provide a cure that is sufficiently prolonged and free of complications to warrant human studies. This should be a minimum requirement if the urgency of work on human embryonic stem cells is to be accepted in the face of the ethical barrier.
> *Emeritus Professor Jack Martin, University of Melbourne (Submission LRC552)*

Emeritus Professor Martin stated that he considers the benefits of treatment from prospective ES cell therapies have been exaggerated, that there has been no proof of concept in any animal model of disease, and that there are significant safety issues that would rule out the possibility of any clinical trials. Professor Martin also did not consider that research has been held back by the current legislation. There are many animal models that mimic the diseases involved (eg for Parkinson's disease) that could be used to demonstrate efficacy and safety. So far, using these animal models, ES treatments have caused partial improvement, but these improvements have been short term and there have always been safety issues (such as teratoma formation):

> Malignant tumour formation is a major complication of ES cell transplantation. The propensity to develop teratomas has been a feature of all the animal studies so far with ES cells — tumours having been associated with ES cell transplantation into the pancreas for diabetes, into the brain for Parkinson's disease, and into the heart for heart muscle damage. In the latter case also serious abnormalities of heart rhythm have occurred, a complication not encountered with adult stem cells used for the same purpose. There has been virtually no progress in understanding the causes of this propensity of ES cells to develop tumours, and until that is resolved there can be no question of moving to therapeutic use of ES cells in human subjects. The tumour complication has not to the present time been a feature of the use of adult stem cells.
> *Emeritus Professor Jack Martin, University of Melbourne (Submission LRC552)*

Finally, Professor Martin also asserted that disease modelling work should first be undertaken in animal models and only be considered for application to humans when much more is known about its potential.

Professor Alan Harvey (appearing at the Perth hearings with representatives of the Western Australian Reproductive Technology Council, but speaking for himself as a scientist involved in fetal transplantation for many years) agreed with this position and said that he thought it important for the Committee to hear from scientists from all sides of the debate. He was personally in favour of some ES cell work, but stressed that many aspects, such as culture conditions and developmental stages, remained to be worked out before any further changes to the legislation could be considered:

> I'm in favour of embryonic stem cell work in association with adult stem cell work but my considered view is that there is a great deal we don't understand about embryonic stem cells, about what drives their differentiation … what will happen to them after transplantation. It will take a long time to work out and in that context to go into therapeutic cloning at this stage is premature. *Professor Alan Harvey, Western Australia (Perth hearings)*

At the Brisbane hearings, Professor Michael Good, Director, Queensland Institute of Medical Research, also told the Committee that the human ES cell lines currently derived from excess ART embryos would be unlikely to be used in clinical trials for cellular therapies because of problems of immune rejection:

> … the vast majority of tissues derived from IVF embryos will not implant … and result in alleviation of human suffering. They won't implant because they will be rejected by the immune system unless they are perfectly and correctly matched with the recipient. The molecules which are responsible for graft rejection are many … There are millions of different combinations and unless a combination is correct a tissue will be rejected by the immune system, which is a very powerful means of rejection. *Professor Michael Good, Queensland Institute of Medical Research (Brisbane hearings)*

However, other researchers have stressed that mechanisms are being developed to overcome such immune rejection, at least for some of the diseases of interest for cellular treatments. For example, at the Sydney hearings, Dr Kuldip Sidhu, Chief Hospital Scientist, Diabetes Transplant Unit, Prince of Wales Hospital, told the Committee that, in the case of treatment of insulin deficiency for type 1 diabetes, the transplanted cells can be contained in specifically designed capsules that shield the cells from immune rejection but allow the release of insulin. Dr Sidhu said that this has already been done in an animal model.

Some submissions described recent developments in the use of AS cells. Most described how AS cells can be induced to differentiate into other cell types. Professor Mackay-Sim (Eskitis Institute of Cell and Molecular Therapies, Griffith University) described his work on neural stem cells from the human nose (olfactory cells). These cells, which are easily obtained from the nose, have been grown in culture and differentiated into many cell types, which is a characteristic of pluripotent stem cells:

> In our lab we have isolated an adult stem cell from the organ of the sense of smell in the human nose. These are neural stem cells, related to those found in the brain, which seem to preferentially form neurones and glia, the cells of the nervous system. We have, however, been able to induce these adult stem cells to become liver cells, heart cells, muscle cells, kidney cells, blood cells, fat cells and numerous other cell types … *Professor Alan Mackay-Sim, Eskitis Institute of Cell and Molecular Therapies, Griffith University (Submission LRC217)*

At the Brisbane hearings, Professor Mackay-Sim stressed that the pluripotent nature of some AS cells makes them suitable for development of autologous therapies (because they can be taken from the same patient who needs the cellular treatment), as well as disease progression and drug development studies. He also noted that AS cells do not grow in such an uncontrolled manner as ES cells (and therefore do not give rise to teratomas). Finally, he said that the cells are exact copies of the person from whom they are extracted, whereas a cloned cell is not an exact replica because the cytoplasm and mitochondrial DNA of a cloned cell come from another person. However, Professor Mackay-Sim said he had not ruled out the need for ES cell research, and that he could not say which lines of research are more likely to succeed (see below).

Professor Mackay-Sim's group is also doing a phase 1 clinical trial using olfactory ensheathing cells for treatment of paraplegia. These cells are specialised cells rather than AS cells, but such studies provide further confirmation of the potential for cellular therapies in general and illustrate that not all cell transplantation repair will require stem cells.

Support for ES cell research

Many ES cell researchers, other scientists and scientific organisations who made submissions, attended the public hearings or discussion forums, or met with the Committee during site visits supported the continuation of human ES cell research (with appropriate safeguards). For example:

> My experience, relating to research that is being done at the Diabetes Transplant Unit and from reviewing the literature, has left me with no doubts that human embryonic stem cells are extraordinarily valuable and have the potential in time to bring great benefits to our society.

> Although the therapeutic potential will most likely be seen over the long term, the advances that are currently being made in basic research are significant. *Mr Justin Lees, Diabetes Transplant Unit, Prince of Wales Hospital, Sydney (Submission LRC441)*

> Human cells, whether derived from cloning techniques, from embryonic stem (ES) cell lines, or from primordial germ cells, should not be precluded from use in approved research activities in cellular and developmental biology. *Australian Academy of Science (Submission LRC18)*

> … we should not 'close the door' on embryonic stem cell research (with appropriate safeguards) until we know adult stem cells have at least as good a potential for treating the vast range of problems facing clinical medicine. I urge the Committee to keep open the opportunity for maximizing recovery and alleviating suffering by allowing embryonic stem cell research and nuclear transfer under suitable controls.
> *Professor Phil Waite, New South Wales (Submission LRC321)*

These respondents also stressed that, in addition to the much publicised use of ES cells for the development of cellular therapies, there are also potential uses of ES cells for studies of diseases and testing drugs. Most of these contributors believed that research on AS and ES cells should continue in parallel:

> … embryonic stem cell research should be viewed as complementary to adult stem cell research. Both avenues of investigation hold promise which when explored together will lead to a better understanding and development of stem cell-based human therapeutics.
> *Stem Cell Sciences Ltd (Submission LRC318)*

> … we see research involving hESC to be only one component of stem cell research. Research using stem cells from non-embryonic sources also needs to be encouraged, and we congratulate the Catholic Church in financially supporting this endeavour.
> *Diabetes Transplant Unit, Prince of Wales Hospital, Sydney (Submission LRC180)*

This view was also shared by AS cell researchers. For example, AS cell researcher Professor Mackay-Sim, Eskitis Institute of Cell and Molecular Therapies, Griffith University, commented:

> Advances in one technology do not suggest it is necessary to cease exploring another. In the case of adult stem cells and embryonic stem cells, knowledge of the one will illuminate knowledge of the other but the ethical issues raised by the embryonic stem cell debate should be informed by knowledge of alternative technologies. *Professor Alan Mackay-Sim, Eskitis Institute of Cell and Molecular Therapies, Griffith University (Submission LRC217)*

Although he also believes that AS cells are likely to replace ES cells:

> It is probable that such [adult] stem cell lines will render therapeutic cloning irrelevant and impractical. *Professor Alan Mackay-Sim, Eskitis Institute of Cell and Molecular Therapies, Griffith University (Submission LRC217)*

At the Sydney hearings, Professor John Rasko, Group Head, Gene and Stem Cell Therapy, Centenary Institute of Cancer Medicine and Cell Biology, and Royal Prince Alfred Hospital, told the Committee that his work was predominantly with AS cells but that he also followed developments in ES cell work. Associate Professor Rasko noted that his group had not applied for a licence for ES cell work because it was a difficult and time-consuming process and ES cell work was not their focus, but suggested that he would welcome the opportunity to do comparative studies with adult and embryonic stem cells were it easier to gain access to ES cells.

The theme of collaborative work in the two disciplines was also raised by Dr Teija Peura:

> … these fields support each other instead of being opposite propositions. Information gained from embryonic stem cell research will most certainly benefit all stem cell research … Hence abandoning this promising area of research now would be very shortsighted and scientifically unsound. *Dr Teija Peura, New South Wales (Submission LRC781)*

At the Melbourne discussion forum, Dr Megan Munsie (Stem Cell Sciences Ltd) noted that Dr Gesine Kögler published work on cord blood stem cells (Kögler et al 2004) after visiting the laboratories of ES stem cell workers and learning some of their techniques.

Some submissions asserted that AS cells have more limitations than ES cells in terms of their plasticity and can be difficult to collect and grow. For example, Mrs Heather Payne, Victoria (Submission LRC534) provided information from Dr Wise Young, WM Keck Center for Collaborative Neuroscience, United States, stating that recent work suggests that AS cells may also be useful but are difficult to isolate and expand, and have not yet been shown to replace neurones in the central nervous system.

Dr Gail Tulloch, Key Centre for Ethics, Law, Justice and Governance, Griffith University, said:

> This is probably THE most controversial point: whether adult stem cell research displaces embryonic stem cell research, or whether there is room for both. Dr Catherine Verfaillie of the University of Minnesota (the researcher whose pioneering work was published in *Nature* in June 2002), points out the serious scientific limitations of adult stem cells, and how hard they are to grow into heart tissue, and that they are harder to collect than embryonic tissue and likely to be very expensive. As she said, 'It doesn't mean that you should close other avenues of research … It may suggest one cell is better at one thing, and another at something else … We should be able to study both and ultimately let the science decide which will be best for treatment.' *Dr Gail Tulloch, Key Centre for Ethics, Law, Justice and Governance, Griffith University (Submission LRC315)*

There were some criticisms from the community that researchers had failed to deliver the cures for disease that were promised at the time of the debates in 2002. In response to these concerns, respondents noted that there had been very little time since the legislation was debated and passed (2–3 years) and it is much too soon to be making judgments about the level of progress. Most researchers agreed that progress was about in line with expectations within the scientific community and that they would not expect significant progress, particularly for clinical cellular therapies, for at least another 5–10 years. Clearly, further research on growth and differentiation of human ES cells is needed, as well as further properly constituted preclinical studies of efficacy and safety.

At the Melbourne hearings, Professor Simon Carroll, representing AusBiotech, stressed that uses of human ES cells for study of disease models and for drug testing are also in the early stages of development because researchers are still grappling with how to grow human stem cells. He noted that mouse ES cells have been used to generate neuronal cells, which are being used to screen drugs for Alzheimer's disease.

Representing the Australian Academy of Science, Professor Bob Williamson, speaking at the Melbourne hearings, also stressed this point:

> We do not have a clue whether all children with Type 1 diabetes have a similar aetiology or not. We do not know why it has doubled in the past 15 years; we do not know why those cells are dying back … And none of the animal models are really that good … And so we have a very clear need of it in that case. Another example is Parkinson's … These are examples where we only detect the patient when the disaster has happened and we don't understand.
> *Professor Bob Williamson, representing the Australian Academy of Science (Melbourne hearings)*

Also representing the Australian Academy of Science at the Melbourne hearings, Professor Suzanne Corey stressed that:

> … it's very dangerous to overstate these technologies because there's a long way to go to using them efficiently and effectively to cure disease. But there is absolutely no chance that we will get to that position of really making a difference to these diseases unless we walk down this path of research and that's why I feel very passionately that this research should be allowed under appropriate conditions that the community feels comfortable with at this point in time …
> *Professor Suzanne Corey, representing the Australian Academy of Science (Melbourne hearings)*

Support for ES cell research was not confined to the scientific community. People affected by diseases that may potentially be treated with ES cells supported the continuation of research with ES cells. One mother of a family with several members affected by autoimmune disorders (including two sons with type 1 diabetes) said that, although they did not support human cloning, they supported the continuation of ES cell research, which will hopefully lead to stem cell therapies (Confidential submission LRC216).

Another submission, also from a mother of a child with type 1 diabetes, said that, should a cure for diabetes be found, only stem cells specifically created for research (by any means) would be able to meet the demand for cells to treat the growing numbers of diabetics, as well as to supply the needs of researchers (Confidential submission LRC403).

Other researchers stressed that the creation of nuclear transfer (cloned) embryos would allow derivation of patient-specific stem cells. These cells would not be rejected on transplant back to the person for whom they are created, and this is the main reason that researchers want to develop this technology (see Chapter 6 for further discussion of this issue).

At the Perth hearings, Mr Richard Egan, State President, National Civic Council, and Western Australian Coordinator of Do No Harm: Australians for Ethical Medical Research, agreed that the key to consideration of lifting current restrictions would be further success in animal models. Also, because there is still a large stockpile of excess ART embryos that are available for research, Mr Egan maintained that it is not the legislation stopping this research but, rather, problems in the nature of the material.

Further discussion of community attitudes is included in Chapter 7.

Alternatives to embryonic stem cells

Various sources of adult stem cells and other cellular treatments were put forward as alternatives to ES cells. These included:

- human cord blood, umbilical cord, placenta and amnion (Caroline Chisholm Centre for Health Ethics Inc, Submission LRC392)
- multipotent adult progenitor cells from the bone marrow (a subpopulation of mesenchymal stem cells) (Stem Cell Sciences Ltd, Submission LRC318)
- mesenchymal stem cells (Caroline Chisholm Centre for Health Ethics Inc, Submission LRC392)
- stem cells from the maxillary cancellous bone (MYO Australia, Submission LRC393)
- olfactory ensheathing cells (for treating spinal cord injuries) (Professor Alan Mackay-Sim, Queensland, Submission LRC217).

Some respondents also proposed potential alternative technologies to avoid the use of human ES cells:

- Altered nuclear transfer-oocyte assisted reprogramming, which is a method being developed to convert AS cells into ES cells by genetic reprogramming (Dr Arthur Hartwig, Queensland, Submission LRC207).
- Other non-stem cell transplantations (such as the ‘Montreal Protocol’ for using pancreatic beta cell transplantation for type I diabetes) (Professor Alan Mackay-Sim, Queensland, Submission LRC217).
- Human embryonic germ cells derived from ectopic fetuses 5–9 weeks after fertilisation without the need for a deliberate induced abortion (Caroline Chisholm Centre for Health Ethics Inc, Submission LRC392).

- Inactivation of the gene responsible for development of functional trophoblast cells, necessary for implantation and ongoing development of the blastocyst. Such entities will not be capable of implantation and ongoing embryonic development and therefore, it is argued, would not be considered to be embryos (Caroline Chisholm Centre for Health Ethics Inc, Submission LRC392).

5.4 Summary — developments in stem cell sciences

Embryonic stem cell research has been extremely active since 2002, 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 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. Two cell lines already derived, MEL 1 and MEL 2, have been accepted by the UK Stem Cell Bank and will be available for researchers internationally.

Research using stem cells from non-embryonic sources (adult stem cells) has also advanced since 2001, including identification of AS cells from many more tissues and further evidence that some AS cells may be pluripotent. However, mechanisms of transdifferentiation are not well understood and in some cases are disputed. Culture conditions for growing well-characterised AS cells are being developed as for ES cells.

Development of stem cell therapies (ES cells and AS cells) is a very active area of research covering many diseases, conditions and injuries. ES cell research is mainly confined to preclinical (animal) studies because the cells are not yet characterised well enough for use in clinical trials and there are significant risks (such as tumour formation). The scope of AS cell research is also very broad, and many cell types are being studied, with some progressing to preliminary clinical trials. Australian researchers are actively engaged in work on stem cell therapy research with both AS and ES cells.

ES cells also provide good models for basic disease research. Although this has not yet been extensively tested, researchers feel that the use of ES cells (particularly those derived by nuclear transfer technologies from people with genetic diseases) would provide many opportunities for understanding disease progression, as well as for testing new drugs and other chemical agents for their pharmacological action, toxicity and genotoxicity. AS cells could also be used to develop similar model systems.

These developments have continued to highlight moral and social questions about the use of human embryos in research. Indeed, it was clear to the Committee that much of the debate regarding the relative merits of ES and AS research was underpinned by differing attitudes towards the moral status of human embryos, and at times it was difficult to distinguish moral arguments from scientific or biological ones. This requires that all arguments be carefully examined not only in terms of the accuracy or lucidity of the argument itself, but also in terms of the values or interests of the individual or group making the argument. This is the focus of Chapter 7.

6 Developments in medical and scientific research: human cloning

6.1 Background to cloning research

Definitions and terminology

The terms ‘clone’ and ‘cloning’ have been used in the scientific literature to describe many types of genetic copying, from copies of sections of DNA (genes) to copies of plants (in agriculture) and cells cultured in a laboratory. The term first came to public prominence in connection with copying a whole animal, however, after Dolly the sheep was born in the late 1990s, thus highlighting the theoretical possibility that a cloned human could be created using the same technology.

Public discussion of human cloning is complicated by the fact that cloning technology, including the distinction between cloning to form a new individual and cloning to obtain embryonic stem cells (ES cells), is complex and therefore not well understood.

Cloning of animals, including humans, involves the removal of the nucleus from an egg, and its replacement with genetic material from a donor somatic cell (that is, any cell in the body apart from eggs, sperm, or their precursors). The reconstituted egg cell is then activated using various methods to reprogram the transferred nucleus back to an embryonic state, thus causing initiation of embryonic development. Usually, the transferred nucleus is from a somatic cell, but it can also be from another source, such as an ES cell. The new entity formed is a genetic copy (clone) of the individual from whom the cell nucleus came.

This technique, which is banned in Australia under the PHC Act, is usually known as somatic cell nuclear transfer (SCNT), but is also referred to as ‘nuclear transfer’, ‘cell nuclear replacement’ or other similar terms. In the case of mammals, the cloned embryo so formed can either be transferred into the uterus of a female, where it may undergo complete gestation and birth (reproductive cloning), or it can be cultured to the blastocyst stage and then disaggregated to obtain the inner cell mass, which is them cultured to derive ES cells for use in research and/or treatment.

The latter use has generally been referred to as ‘therapeutic cloning’, on the basis that the ES cells derived are used for the development of stem cell therapies (and, ultimately, if the research is successful, as the therapeutic product itself). However, this term is not universally accepted because the procedure involves destruction of the embryo (that is, it is not therapeutic for the embryo). ‘Nonreproductive cloning’, ‘cloning for research purposes’, ‘adult cell reprogramming’ and ‘nuclear transfer’ are all alternative terms for the procedure, but none of these terms is widely used. In this document, the Committee has used the terms ‘therapeutic cloning’, and ‘cloning to generate embryonic stem cells’ to describe this area of research and ‘nuclear transfer’ (including SCNT) for the technology most commonly used to create an embryo clone.

Under the PHC Act (see Section 2.1), the entity formed by nuclear transfer is called a human embryo clone. Other entities also included in the definition of a human embryo clone under the Act include embryos formed by embryo splitting, nuclear transfer using non-somatic cells (such as ES cells) and parthenogenesis (see Section 4.3).

Reproductive cloning of humans is considered unacceptable throughout the world because of ethical concerns about the social and psychological implications of creating a copy of a living or dead person, and safety issues associated with the technology. Like Australia, many other countries and jurisdictions have passed legislation or introduced regulations to ban reproductive cloning (see Section 2.6). It is also not supported within the scientific community.

However, cloning to generate ES cells has been much more controversial. Some countries (including the United Kingdom, the United States, South Korea and Singapore) have allowed the use of the technology on the grounds that there are potential benefits of research for people with incurable conditions and injuries, while others (including Australia) have banned it on the grounds that creating embryos to destroy for research is not ethically acceptable (see Section 2.6 for further information on international legislation and conventions).

Animal cloning

Reproductive cloning of animals has clear applications in agriculture for the rapid production of highly valued stock, and in preclinical scientific and medical research for the production of animals of known genotype. This enables the elimination of genetic difference as a variable, and also assists research that seeks to understand the interactions between the various components of the cell, and the effects of genetic programming over time. However, the development of efficient and more refined techniques for producing healthy cloned animals has been slow over the past 20 years.

From the late 1990s, cloning technology in animals (mainly SCNT) produced live offspring in sheep, cattle, goats, rabbits, cats and mice, although it has been less successful in dogs, rats and primates. However, the technology is inefficient (in terms of the number of nuclear transfers that are required to produce one viable embryo) and has been accompanied by developmental and health problems at all stages from the embryo to postnatal stages and also in later life.

Human cloning

By 2001, cloned animal embryos had provided stem cell lines of research interest and usefulness, and the possibility of extending this work to human clones was being widely suggested. Therefore, although there was a desire to ban human reproductive cloning, there was a growing demand from researchers to use cloned human embryos as a source of stem cells for transplantation. Other potential uses of ES cell lines from human embryo clones were also identified, including creating ES cell lines from a person with a particular disease to provide a model for study of the cellular development of that disease, and testing of drugs and other chemical agents for their pharmacologic or toxic effects on specific cell types with or without a disease genotype.

However, although the idea of ‘therapeutic cloning’, or cloning to generate stem cells, was widely reported in the media in 2001, no viable cloned human embryos had yet been created from which to obtain stem cell lines. In that year, some researchers in the United States claimed that they had created six-cell human embryo clones, but the claim was unsubstantiated. The same researchers also attempted to create parthenogenetic embryos to the blastocyst stage in order to obtain stem cells, but these attempts were not successful.

Review findings

The remainder of this chapter summarises the findings of the literature review referred by the Minister for Ageing for cloning research since 2001 (Biotext 2005; see Section 3.3) and the other information received by the Committee during the reviews. The focus of the chapter is on the development of cloning technologies and the creation of patient-specific stem cells derived from human embryo clones (so-called ‘therapeutic cloning’).

A review of stem cell research in general terms, including differences between embryonic and adult stem cells, is included in Chapter 5. The biological definitions of a human embryo and human embryo clone are discussed in Chapter 8, and community attitudes to embryo research and cloning are discussed in Chapter 7.

6.2 Literature review — developments in human cloning since 2001

Further details from the literature review, including methods, results of the searches and all relevant scientific references, can be seen on the Legislation Review website.[20]

Developments in animal cloning

Since 2001, to improve cloning outcomes, researchers have worked to understand normal developmental processes and how they are disrupted during nuclear transfer, and also to improve the activation methods used during nuclear transfer.

Embryo splitting is another way to create clones; in humans, this happens naturally during the formation of monozygotic twins. Embryos can be split at the cleavage, morula or blastocyst stage, and this technique has been used in mice, rats, rabbits, sheep, cows and pigs. Due to difficulties in using nuclear transfer techniques in nonhuman primates, embryo splitting has been investigated in rhesus monkeys as an alternative cloning method (Schramm and Paprocki 2004).

Parthenogenesis is reproduction without genetic contribution by a male or meiotic female chromosome reduction. While mouse parthenotes can develop past implantation, primate parthenotes can only develop to blastocyst stage, and have been used to derive primate stem cells (Cibelli et al 2002, Vrana et al 2003).

Developments in nuclear transfer

To improve cloning outcomes in animals, researchers have aimed to minimise the impact of nuclear transfer techniques by using the following approaches:

- Understanding normal developmental processes and how they are disrupted during nuclear transfer, such as:
  - chromatin remodelling — there is a genome-wide decrease in histone acetylation, and variable telomere elongation, resulting in abnormal chromatin structure
  - DNA methylation imprinted genes — DNA methylation levels and patterns are variable, and there is a lack of the imprinting that occurs during natural fertilisation due to the contribution of both a maternal and a paternal genome
  - gene expression — levels of the expression of genes important for development are variable
  - oocyte cytoplasm — factors such as mitochondrial DNA can affect cloning efficiency and development at later stages of animal development (fetal development).
- Improving the physical methods used during cloning, such as:
  - enucleation methods — physical and chemical enucleation methods can damage the embryo, so noninvasive methods are being developed
  - fusion and activation methods — cloned embryos are usually reconstructed with fusion and activation processes that require long manipulation times
  - culture medium — culture media have improved
  - efficiency and cost (in livestock production) — some research, driven in particular by livestock industries, has focused on reducing the need for expensive equipment for nuclear transfer.

20. See http://www.lockhartreview.com.au

(These findings are based on many review articles in this very active field of research; see the full literature review for further details.)

Recent developments in cloning animals

By researching molecular mechanisms underpinning reprogramming and refining nuclear transfer techniques, researchers have been able to improve cloning outcomes in animals:

- In pigs, cloning efficiency has been increased by developing a method for the injection of whole cells, thus reducing the manipulation time of donor cells and recipient oocytes.
- In nonhuman primates, modifications to methods (including enucleation, fusion and culture medium) used to clone a human embryo (see below) were applied to clone monkey embryos to the embryo transfer stage.
- In mice, researchers used expression of a key embryonic gene that is expressed in pluripotent embryonic cells, but silent in somatic donor cells, to determine the developmental potential of clones at the preimplantation stage.
- In cattle, chromatin in the donor somatic cell nucleus was remodelled before it was transferred into the recipient oocyte, improving cloning outcomes.

Work on interspecies nuclear transfer has continued, with various combinations of species used to investigate techniques for cloning and the effects of cloning on normal developmental processes. Some of this work may also help clone endangered species, where there are low numbers of available oocytes and surrogates.

Building on the interspecies cloning work in animals, and to overcome difficulties in sourcing human oocytes, some researchers overseas have used animal oocytes in nuclear transfers with human nuclei to create ‘human’ embryos (Chen et al 2003). These embryos could be used to derive human ES cells. However, most countries do not allow the creation of hybrid or chimeric embryos involving human tissue.

Developments in human cloning

The first report of human embryo cloning to appear in a peer-reviewed scientific journal was in 2004 (Hwang et al 2004). South Korean scientists cloned human embryos until the blastocyst stage to create ES cells. In 2005, the same group of researchers applied these nuclear transfer methods to clone human embryos using somatic cell nuclei from patients who have various diseases or injuries, to derive ‘tailor-made’ stem cell lines (Hwang et al 2005).

Also in 2005, researchers in the United Kingdom showed that nuclear transfer can be achieved in human oocytes using heterologous donor nuclei and surplus and donated oocytes (Stojkovic et al 2005). Other researchers are attempting to produce patient-matched ES cells by fusing the somatic cell nuclei from patients with ES cells. One United States–based group has claimed to have achieved this (and called the resulting cells ‘stembrids’). This research has not yet been published in the peer-reviewed literature.[21]

In light of the advances that have been made in the creation of human ES cells from cloning techniques, it has become critically important to fully understand the genetic changes that occur during cloning. This is because if embryo clones have genetic defects, then stem cells derived from those embryos could also have the same defects. Research aimed at elucidating the genetic consequences of cloning is currently being conducted in a number of centres, and the results of this research are likely to be enormously significant to the entire field.

21. See http://www.newscientist.com/channel/sex/mg18625014.100

6.3 Submissions and hearings on human cloning

Use of the terms 'reproductive' and 'therapeutic' cloning

Some respondents cautioned against the use of the term 'therapeutic cloning'. For example, at the Brisbane hearings, Associate Professor Melissa Little, Institute for Molecular Bioscience, University of Queensland, said that she strongly supported the change in terminology recommended by the International Stem Cell Association, to 'nuclear transfer'. She said this term is preferable because it describes what happens and removes the term 'cloning' (and therefore association with reproductive cloning). Researchers from Monash University, Melbourne, agreed:

> The SCNT procedure was formerly often referred to as therapeutic cloning. This terminology has been banned by the scientific community, because it is inaccurate and misleading. The procedure in and of itself is not therapeutic … *Dr Martin Pera and others, Monash University (Submission LRC509)*

The NHMRC (Submission LRC790) stressed that it has replaced the term 'therapeutic cloning' with 'cloning for research purposes' in all its documentation. However, this latter term restricts the technology to research and does not include the potential use of ES cells derived from nuclear transfer embryos as cellular therapies.

Others stressed that there needs to be a clear distinction between prohibited reproductive practices and practices that are useful for research and therapy:

> The *Prohibition of Human Cloning Act 2002* and the *Research Involving Human Embryos Act 2002* must be amended to define 'cloning' technology and clearly distinguish between the use of this technology for sound research endeavours involving the generation of embryonic stem cell lines and prohibited reproductive purposes. *Stem Cell Sciences Ltd (Submission LRC318)*

Several others did not think that such a distinction is morally or biologically defensible. For example:

> Distinctions between 'therapeutic' and 'reproductive' cloning must be rejected as spurious and dishonest. *Mr Bruno and Mrs Margaret D'Elia, Victoria (Submission LRC639)*

> Although some would wish to make a distinction between therapeutic and reproductive cloning, this distinction is not biological and only has a sociological basis, not a scientific basis … As there is no developmental difference, the only possible difference is that of intended use, and intention is not always a robust or objective enough category upon which to legitimate a practice. *Anglican Church of Australia, Sydney Diocese (Submission LRC780)*

Some respondents noted that this position is supported by the United Nations resolution passed in March 2005 prohibiting all forms of human cloning. Australia voted in favour of this resolution. The United Nations position was, in part, based on an assertion that it would be impossible to police a ban that prohibited reproductive but not therapeutic cloning. Embryos produced by either method are morphologically identical, and inspectors would be unable to detect infringements in an assisted reproductive technology (ART) clinic setting.

At the Adelaide hearings, Associate Professor Wendy Rogers, Department of Medical Education, Flinders University, thought that it would be helpful to make greater distinction between therapeutic and reproductive cloning based on the intention behind creating the clones:

- therapeutic cloning — to create a cell line
- reproductive cloning — to create a human.

At the Sydney hearings, Reverend Dr Andrew Cameron and Reverend Dr Andrew Ford, Anglican Archdiocese of Sydney, stated that intention is not a robust enough reason to make the distinction between the two uses. As reproductive and therapeutic cloning are based on exactly the same technology, they felt that use of one will inevitably lead to use of the other.

At the Melbourne hearings, Ms Margaret Tighe and Dr Mathew Piercey, representing Right to Life Australia, also stated that there is no scientific basis for the different terms, because they describe the same procedure. In both cases it involves creation of a human embryo and therefore, from a moral perspective, it is the same. Mr Gerard Calilhanna, New South Wales, shared this view:

> However, the concepts of 'Reproductive cloning' and 'Nonreproductive cloning' are disingenuous. Both imply a type of 'back door' justification of cloning as the concept of cloning is, in essence, indivisible.
> *Mr Gerard Calilhanna, New South Wales (Submission LRC254)*

Reproductive cloning

In line with prevailing community attitudes around the world, most respondents to the reviews supported the continued prohibition of human reproductive cloning. Ethical concerns about reproductive cloning, such as the social and psychological implications of creating genetic copies of other living or dead individuals, as well as concerns about eugenic-style selection of individuals with particular genetic characteristics, were usually not stated in detail, because these concerns were assumed to be widely accepted and supported in the community.

In some cases, concerns about eugenic use of reproductive cloning reflected concerns about gene technology in general:

> The quest for genetic enhancement of offspring is the most virulent form of the new eugenics … One day, when genetic tests are more widely available, it might become illegal to bring into the world a child with a genetic disability. (I understand already in the U.S., some Health Insurance schemes limit their liability in the event of a child with an intra-uterine diagnosable disorder, to the cost of an abortion.) *Dr Arthur Hartwig, Queensland (Submission LRC207)*

A few respondents, while supporting the ban on reproductive cloning, stated that reproductive cloning was less objectionable than cloning for stem cell research or therapeutic purposes because these involve destruction of an embryo. Mr Malcolm Lambert, Tasmania (Submission LRC343), said that because we accept identical twins we should also accept cloned humans. The only difference is that the person and their identical sibling would be born years apart, rather than minutes apart.

Scientific reasons for continuing the ban on reproductive cloning included serious safety issues:

> Aside from the obvious ethical concerns, the consistently high rate of miscarriage, premature birth and developmental deficiencies in animal 'cloning' studies dictate the inherently unsafe nature of cloning technology for the purposes of reproduction.
> *Stem Cell Sciences Ltd (Submission LRC318)*

> The problem of developmental defects is a much more serious objection to human cloning. My numerous experiments resulted in 3 cloned sheep and all three had phenotypes that were abnormal compared to progeny born by conventional reproduction. These abnormalities included large birth weights, feeding problems, endocrine and immunological deficiencies and suspected abnormalities of behaviour. Some or all of these have also been documented in the literature from other laboratories and in my opinion are associated with abnormal development due to imprecise reprogramming of the genome of the initial nuclear transfer-derived zygote.
> *Dr Kevin Ward, New South Wales (Submission LRC310)*

Other objections to reproductive cloning put forward included problems with genetic parentage and loss of genetic diversity. For example:

> … cloning would be a poor method indeed for improving on the human species. If widely adopted, it would have a devastating impact on the diversity of the human gene pool.
> *Industrial and Social Research Associates Pty Ltd (Submission LRC388)*

Cloning to generate embryonic stem cells

Many respondents thought that creation of human embryo clones to generate ES cells should also continue to be banned. One objection was on the grounds of safety:

> The problem … with the approach of using nuclear transfer to establish a stem cell line is the difficulty of determining if the stem cells derived by this approach are sufficiently normal to allow their use as therapeutic agents in human medicine. In particular, it must be determined whether these stem cells are free of the coding deficiencies that manifest themselves as developmental problems seen in most embryos and foetuses generated by nuclear transfer … Experience would nevertheless suggest that many of these embryos are not normal as judged by their subsequent inability to produce or maintain a normal pregnancy or to produce progeny with a normal physiology. This raises the question whether such abnormality is likely to affect the performance of a stem cell in any proposed medical therapy … The dilemma is that it is hard to see how this can be determined except by experimentation on human subjects and I believe the risks of such experiments at present may be too great to allow them to be carried out. *Dr Kevin Ward, New South Wales (Submission LRC310)*

Another objection was the possible spread of viral infections due to the use of animal products in the culture media of ES cells:

> In growing the embryonic cells in the laboratory the culture medium used is based on biomatter from animal species and carries with it the serious risk of spreading new viral infections from animals to humans. *Dr John Broomhead, New South Wales (Submission LRC372)*

A further objection was the difficulty of monitoring and policing of this activity, increasing the chance of the use of the technology for reproductive cloning:

> … the creation of cloned human embryos and the refinement of techniques associated with their production will make it easier for reproductive cloning to occur … This is a reality that must be faced squarely by those who advocate therapeutic cloning rather than simply denying the strength of the connection. *Southern Cross Bioethics Institute (Submission LRC451)*

These reasons were usually underpinned by stated or unstated moral concerns about the creation and destruction of a human embryo for research or medical purposes:

> … if therapeutic cloning were to be allowed, the deliberate creation of cloned human embryos for the express purpose of their destruction would immediately undermine the community standard that embryos only be created for infertility treatment.
> *Southern Cross Bioethics Institute (Submission LRC451)*

> This is completely opposed to the dignity of the human being, and cannot occur without deleterious effects upon the integrity of our nation, the integrity of human research and ethical science, and the further commodification of unborn human life already inherent in the IVF programmes. *Queensland Right to Life (Submission LRC376)*

However, many others supported use of the technology. The reasons for supporting cloning for the generation of stem cells included support for research with potential to provide ES cell therapies for serious untreatable conditions. For example, a relative of a child with type 1 diabetes said that lifting the ban on therapeutic cloning would increase the supply of stem cells for research and make it possible to treat patients with autologous tissue (Confidential submission LRC412).

A similar comment was made by a respondent with several family members suffering from autoimmune conditions. She said that SCNT could have a significant positive impact on the lives of sufferers of a range of diseases (eg type I diabetes, cancer, Parkinson's disease, and Alzheimer's disease). She requested that the Committee reconsider all the information about the positive outcomes of SCNT (Confidential submission LRC216).

At the Sydney hearings, Ms Sandra Dill and Ms Debbie Jeffrey, representing ACCESS (a national organisation representing ART consumers), commented on SCNT:

> And I guess just in a general sense we've often wondered why there's been objection to somatic cell nuclear transfer … if for someone who was sick and needed help, and I'm sure others will address this in far more detail who are affected by that, it just seems commonsense to be able to allow that to happen. And perhaps if people sort of thoughtfully looked into it they might perhaps have fewer objections. ... we haven't heard any of our members not support this. *Ms Sandra Dill and Ms Debbie Jeffrey, ACCESS (Australia's National Infertility Network) (Sydney hearings)*

Others commented on the use of SCNT to study disease states:

> The act should be modified to allow research using SCNT procedures to be undertaken. This process will enable the development of individually DNA matched stem cells for treatment, overcoming the problems of tissue rejection and the development of stem cell lines carrying genetic disorders, for researching the causes of such diseases and their treatment. *Dr Peter Williamson, Western Australia (Submission LRC413)*

> If SCNT is legalized in Australia, the DTU would wish to apply for a licence to make SCNT-hESC lines that could be used as model for studying diseases such as Type I diabetes in vitro that may also help in drug discovery. These SCNT-hESC lines will be helpful in studying genetic disorders, especially those that result in cancer. A prime disorder for examination is familial breast cancer, for which young women have both breasts removed prophylactically. *Diabetes Transplant Unit, Prince of Wales Hospital, Sydney (Submission LRC180)*

> SCNT provides researchers with an immediate opportunity to generate disease-specific stem cell lines that could be used to better understand in the laboratory the progression of complex diseases such as diabetes, motor neuron disease, Huntington's and Parkinson's diseases. The use of such stem cell lines in research could also lead to the identification of drugs and/or treatments … *Stem Cell Sciences Ltd (Submission LRC318)*

Others commented on the usefulness of SCNT in screening of new drugs:

> Stem Cell Sciences believes that the use of human embryonic stem cell lines derived from specific disease states could prove of great value to the pharmaceutical industry in initial stage screening of new drug candidates in that it would afford access to and use of unique material …While human stem cells represent an extremely valuable benchmark for drug candidate screening, and have many advantages over using animal cells and cells derived from tissue biopsies, the ability to also use cells derived from a diseased patient would provide a highly specific and useful reagent for not only understanding the molecular aspects of disease development but also the discovery of better medicines that can reach the clinic sooner. *Stem Cell Sciences Ltd (Submission LRC318)*

Referring to some recent research using nuclear transfer to generate new ES cell lines without having to create a human embryo clone (see Section 5.3), some respondents stated that they would support these new approaches to creation of patient-specific ES cells:

> This ban ought to be retained for developing totipotent embryo clones resulting from SCNT. However, the ban need not apply to clonal pluripotent stem cell lines created without the destruction of any genuine human embryos. *Caroline Chisholm Centre for Health Ethics Inc (Submission LRC392)*

> Alternative methods for deriving pluripotent stem cell lines (equivalent to embryonic stem cells) are needed and should be pursued. These alternatives should include cell fusion techniques involving somatic cells and embryonic stem cells and cell extracts or cytoplasm from sources other than human eggs (eg animal eggs and stem cell extracts). These reprogrammed cells would only be used for research to study the causes of diseases and could lead to new drug discoveries that might ameliorate such diseases. Changes to the Act should enable such research. *Dr Martin Pera and others, Monash University (Submission LRC509)*

Many researchers and other respondents admitted that the 'hype' around the potential benefits of ES cells in general, and patient-matched cells in particular, had not been helpful. At worst, this has led to a mistrust of scientists.

However, research progress is likely to continue to be slow until safety concerns and other difficulties are overcome:

> The use of stem cells in medical research has been greeted by genuine enthusiasm by many. Unfortunately, this enthusiasm has often led to an exaggeration of the speed in which stem cell-based therapies will be available. The scientific community needs to remain responsible. Before any stem cells can be routinely used in cell therapy they must be rigorously evaluated for safety and efficacy. Cells derived from embryonic stem cells must be shown to be free from contaminating pathogens and tumorigenic stem cells, and be able to be grown and delivered to the site of interest in sufficient numbers to engraft and restore function to diseased or damaged tissue. *Stem Cell Sciences Ltd (Submission LRC318)*

Researchers agreed that it may be 10 years or more before current research is translated into effective treatments (if any). However, with medical research, such as cancer research, the fact that progress is likely to be slow is not a reason for prohibiting the research altogether. Indeed, Australia's excellent track record in medical research was seen as an indication of the confidence that people could have in the future potential of the research.

At the Melbourne hearings, Emeritus Professor Jack Martin, University of Melbourne, noted that there is not yet enough evidence from basic science and animal studies that cell therapies or other advances based on patient-matched ES cells will be successful. He felt that it will only be justifiable to consider lifting the prohibition on creating human cloned embryos when such evidence exists. He therefore thought that the prohibition should stand for a further period (after which it may have become possible to create patient-matched stem cells without destruction of a human embryo). (See also Section 5.3 for further information on Emeritus Professor Martin's submission.)

At the Sydney hearings, Professor Julian Savelescu, Director, Oxford Uehiro Centre for Practical Ethics, University of Oxford, argued that a better ethical starting point should be to question why we are not supporting this research. He stressed that we need to allow this research to go forward because it has the potential to save lives. If we cause a delay in this research, we may thereby be responsible for the premature deaths of many people. He noted that once we can foresee the consequences of our actions we start to accumulate blame for those consequences.

At the Brisbane hearings, Associate Professor Malcolm Parker, a medical ethicist from the School of Medicine, University of Queensland, stated that the prospect of alleviating a disease is what motivates research, and because of the unpredictability of research, many types of research should be supported.

Implications for Australian research and availability of new therapies

Some respondents commented that continuing the ban on cloning to generate ES cells would put Australian researchers at a disadvantage in terms of exploring possible new treatments for severe clinical conditions:

> In Australia, Stem Cell Sciences has the technology and ability to deliver such a product. While we have laboratories in UK and Japan, where legislation allows SCNT, our Australian laboratory with its proven track-record on human embryonic stem cell derivation and previous experience in animal SCNT, is clearly the most capable team in our international network though currently prohibited from progressing its efforts in this field.
> *Stem Cell Sciences Ltd (Submission LRC318)*

> Denial of access to this technology will severely hamper Australian medical research. Research in many disciplines would benefit from access to disease specific stem cells. It is important for Australian scientists to be able to derive such stem cells from patients with diseases defined by clinical criteria of Australian standards and to allow access to SCNT stem cell lines from overseas (currently not allowed by Customs legislation).
> *Dr Martin Pera and others, Monash University (Submission LRC509)*

However, while some respondents said that it does not matter if the research is not done in Australia, at the Adelaide hearings, Professor Peter Rathjen, Adelaide University, noted that although Australian researchers exchange information with others overseas, this is not the same as having direct access to such research in Australia itself.

This concern was not limited to researchers: potential recipients of cellular therapies expressed concern that, if this research is not done in Australia, they may be disadvantaged in terms of access to any new therapies that are developed:

> CAMRA supports … change to … therapeutic cloning or … somatic cell nuclear transfer … It is possible to pursue these opportunities with legislation that retains clear prohibition of human reproductive cloning. Global community standards have changed. Legislation supporting the ability to conduct this type of research has been enacted in many other countries … While no one believes the answers will be swift such breakthroughs are seen as dramatic … we don't expect a cure tomorrow or maybe even next week and we don't intend to overstate the promise of research, but how can you overstate hope? To ensure that hundreds of thousands of Australians can benefit from potential lifesaving treatments at the earliest opportunity we believe the government needs to allow SCNT research to take place in Australia as soon as possible. *Ms Joanna Knott, representing the Coalition for the Advancement of Medical Research Australia (Sydney hearings)*

States' views

Submissions from several State governments — New South Wales, Queensland and Victoria — supported removing the prohibition on SCNT:

> Research involving the derivation of stem cells and development of stem cell lines through somatic cell nuclear transfer (SCNT) has the potential to address disease and disability posing significant burden of disease to both individuals and the community, and therefore amendment of the legislation to permit SCNT to be undertaken is recommended. *Ministry for Science and Medical Research, New South Wales (Submission LRC1016)*

> The Queensland Government supports lifting the ban on therapeutic cloning because stem cells have the potential to launch a new era of medicine by curing diseases with custom made tissues and organs — resulting in improved quality of life for Queenslanders and people around the world … Whilst there have been enormous developments in medical research involving adult stem cells, this does not replace the need for SCNT research. Both avenues of research should be responsibly pursued to maximise the chances of curing diseases that cause human suffering. However it is important that the ethical issues identified above are addressed in any legislative arrangements allowing therapeutic cloning. *Queensland Government (Submission LRC930)*

> Reproductive cloning should be distinguished from somatic cell nuclear transfer (SCNT; sometimes referred to as 'therapeutic cloning'), which can provide the research tools for improving our understanding of the causes of diseases and informing the development of potential therapies. Victoria advocates the revision of the *Prohibition of Human Cloning Act 2002* and the *Research Involving Human Embryos Act 2002* in a manner that will allow such research to be conducted within Australia, provided it is adequately controlled and focussed exclusively on prevention or cure of disease. *Victorian Government (Submission LRC537)*

However, the Government of Western Australia did not seek a removal of the restriction on SCNT:

> It is noted that when the legislation was debated in the WA Parliament one year ago there was no evidence of support for therapeutic cloning to be allowed in this State. There was also at that time no evidence of widespread community support for therapeutic cloning in WA. On this basis and in light of the current development status of medical and scientific research in the area, WA is not actively seeking change to this aspect of the legislation. It should be noted that this opinion is based on the current circumstances in WA and does not take into account information and technological developments that are occurring in other jurisdictions. *Government of Western Australia (Submission LRC782)*

Regulation of research activities

Many respondents, including researchers and existing national and state or territory regulatory agencies, stressed that, if nuclear transfer and other similar technologies are legalised (for whatever research purpose), each project should be reviewed using a strict regulatory framework similar to that used by the Licensing Committee for research on excess ART embryos.

> Controlled ethically approved SCNT research should be approved to appropriately licensed institutions to ascertain whether this form of technology may prove beneficial in the future. Without the research, we will never know.
> *Dr Stephen Junk, Western Australia (Submission LRC257)*

Finally, some respondents, while supporting a relaxation of the current prohibitions for research and therapeutic purposes, noted that it would be vital to ensure that appropriate safeguards are in place to protect the rights of women who may be asked to donate oocytes.

> We do not hold moral objections in relation to creating SCNT embryos for research per se, provided appropriate ethical safeguards are put in place with regard to the treatment of women from whom the oocytes are harvested … as well as assessment of the overall cost, utility, and equity impact of such research. *Dr Rachel Ankeny, Sydney University, Associate Professor Susan Dodds, University of Wollongong, and Associate Professor Wendy Rogers, Flinders University (Submission LRC515)*

Access to eggs and exploitation of women

A major concern for many respondents in connection with the use of nuclear transfer methods was the numbers and source of the human mature oocytes that would be required to generate the cytoplasmic 'incubators' required for reprogramming the transferred nuclei:

> Where will all the eggs come from if cloning is to be used for therapeutic purposes? Each patient treated would need their own cloned human embryo, requiring thousands of women to 'donate' eggs, undergoing the risks of ovarian stimulation. *National Civic Council (Submission LRC246)*

This concern was heightened by the fact that retrieval of mature oocytes from women is an invasive procedure requiring hormone stimulation. This procedure carries significant risks, including, in very rare cases, infertility or even death (see Section 4.3). In addition, inefficiencies in the current nuclear transfer technology mean that several eggs are required to create each embryo clone. The need for oocytes may therefore lead to the exploitation of vulnerable women through financial or other incentives:

> Another big concern about cloning is where scientists will obtain enough eggs to conduct their experiments. Will they manipulate the poor into selling their eggs? Do these women realise that there is a certain risk involved? What safe-guards would there be for the rights of the women involved? What counselling would be offered to the women on the procedures?
> *Mrs Nola Drum, New South Wales (Submission LRC273)*

Several submissions from State governments also expressed concern about the potential for commodification of oocytes donated for research:

> If SCNT is to be permitted under revised legislation, a supply of human eggs will be sought. Egg donors are exposed to significant medical, physical, psychological and social dangers. It will be mandatory to prevent exploitation of women under such circumstances … The donation of eggs for SCNT research purposes should be voluntary, with no financial inducements permitted, with donors thoroughly informed of the risks associated with donation.
> *Victorian Government (Submission LRC537)*

> A second major concern expressed about SCNT is the need for ova, and the associated potential exploitation of women and risk to their health. For this reason, the donation of eggs for this purpose should be strictly voluntary, with no financial inducements permitted.
> *Ministry for Science and Medical Research, New South Wales (Submission LRC1016)*

> Eggs are needed to create embryo clones, which means women would be needed for egg donation, either from surplus supplies created for ART purposes, or for the express purpose of research. Egg donation carries risks to the health of the donor and is an expensive procedure requiring drugs and medical intervention. Reimbursement for donors is an issue in common with donors for ART procedures, but needs to be addressed in the context of donating for research. There is concern that vulnerable women, such as those trying to achieve pregnancy, will be at risk of exploitation if surplus eggs from ART are able to be donated for research, or if payment for donation is permitted. *Queensland Government (Submission LRC930)*

Some cited the recent experiments overseas as an example of the problem:

> The [South] Korean experiment required an average of 17 human ova for each successfully cloned human embryo. Questions have been raised about the exploitation of the women who 'donated' the ova for these experiments and exposed themselves to the serious risks (including death) of ovarian stimulation to obtain the eggs. *National Civic Council (Submission LRC246)*

> … the [South] Korean human cloning work was strongly criticized by two bioethicists, who warned in the journal *Science* about the exploitation of young women who were used as egg donors … The point is, this problem will remain as long as human eggs are required, which is a necessary element of therapeutic cloning.
> *Southern Cross Bioethics Institute (Submission LRC451)*

(See Chapters 11 and 13 for further information on this issue.)

On the other hand, Dr Bill Watkins, Director, Tasmania IVF, described the situation with respect to altruistic donation of oocytes in more measured terms:

> … it's a big thing to ask [a woman to donate an egg] … but I think once it's fully explained to them … the treatment nowadays it's all outpatient based. The actual physical risks to them are very, very small … we take a very, very cautious approach to stimulating their ovaries … And I would like to think that all my colleagues would take a very similar approach — if someone is donating for altruistic reasons and there's nothing actually in it for them that you'd take a very cautious approach. And look, complications can occur and people have died having IVF but they're exceptionally rare events and they're not going to run into a lot of the severe risks that ovarian hyperstimulation patients do, because they're not going to be getting pregnant themselves and obviously that's much more of a complication if they're stimulated and pregnant … I would warn them that the biggest concern I would have is … if they've donated eggs at a younger age and then they have infertility themselves in the future if they've left it too late … How are they going to feel about that emotionally?
> *Dr Bill Watkins, Director, Tasmania IVF (Hobart hearings)*

While many submissions noted concerns regarding the risks of oocyte donation and the potential for coercion of donors, a number suggested mechanisms by which the notion of altruistic donation could be strengthened in relation to the donation of oocytes for research purposes:

> Access to eggs will remain a rate-limiting factor in the development of this [SCNT] technology. However … well informed female friends or relatives of patients suffering from debilitating diseases would consent to donating their eggs for specific licensed research projects. Furthermore, through improvements in *in vitro* maturation techniques … it is possible that instead of undergoing invasive egg retrieval procedures, women could donate ovarian tissue that could then be used to generate eggs for specific research projects.
> *Stem Cell Sciences Ltd (Submission LRC318)*

Further information on oocyte maturation is in Chapter 4.

At the Brisbane hearings, Professor Michael Good, Director, Queensland Institute of Medical Research, also noted some other potential sources of cytoplasm to 'incubate' and reprogram a nucleus. Three possibilities are:

- cloned human eggs (ie eggs derived from ES cells)
- animal eggs
- some other tissues.

Use of oocytes from animal sources may be acceptable for basic laboratory research projects, but this approach would not be acceptable to most people for derivation of ES cells for human therapeutic use:

> I am very fearful that scientists will begin to see chimeras as a very realistic alternative to the problem of finding enough eggs to conduct their research.
> *Mrs Nola Drum, New South Wales (Submission LRC273)*

Further discussion of donation of oocytes is in Section 11.2.

6.4 Summary — human cloning

Although the concept of reproductive cloning is quite well understood by the community, so-called 'therapeutic cloning' (cloning to generate ES cells) is not well understood. The technology used in both cases involves creation of a human embryo clone by nuclear transfer. In the former case the embryo clone is implanted in a woman's uterus for gestation, while in the latter case the embryo clone is cultured to the blastocyst stage and the cells in the inner cell mass are removed and cultured to derive ES cells. As the cells are matched to the person whose nucleus was transferred, they will not be rejected if they are transplanted back to that person.

Reproductive cloning has been developed in livestock and laboratory animals, where it has legitimate uses to produce animals of known genotype. However, to date, there are significant health issues for the animals produced by this method, and improvements in techniques for producing healthy cloned animals have been slow.

Since 2001, embryological studies in animals and humans have helped to define the molecular processes that occur during cloning by nuclear transfer. This has led to improvements in cloning outcomes in animals, including primates. Interspecies cloning in animals has helped researchers to further understand processes and improve techniques. These improvements in animals helped South Korean researchers to create cloned human embryos to derive ES cells. However, the processes leading to reprogramming and activation of the genetic material are not fully understood, and the potential for development of problems in any resulting stem cells is also not known at this stage.

The PHC Act prohibits the creation of human embryo clones and thus prohibits both reproductive cloning and cloning to generate ES cells. Many researchers, and people with diseases that could potentially be treated with ES cell therapies, would like the prohibition on cloning to generate ES cells to be lifted. Others find it unacceptable to create human embryo clones specifically to destroy for research or therapeutic uses.

Obtaining human oocytes to use for nuclear transfer is considered a serious matter both by those who would like the current ban lifted and by those who wish to retain it. Those who want to retain the ban cite the issue of oocyte supply and the possible exploitation of women as one of the main reasons for retaining the ban. Those who would like the current ban to be lifted believe that it would be possible to ensure that women are protected by good ethical oversight of oocyte donation and retrieval processes. Also, researchers suggested that this is a short-term problem because techniques are being developed to use cytoplasm from other cell types to incubate and reprogram the transferred nucleus.

Further discussion of community opinion about the creation of embryos for research is included in Chapter 7.

7 Community standards on status and use of embryos

7.1 Introduction

As regulation in research and clinical practice involving assisted reproductive technology (ART) and embryonic stem cells has moral and social dimensions, the legislation and the terms of reference for these reviews require the Committee to take account of 'community standards', a concept that includes beliefs, values, expectations and preferences. However, the Committee has observed that Australian society is composed of many 'communities', each of which may have differing perspectives, interests and values. Furthermore, the standards evidenced by these communities may not be articulated or developed, may differ between individual members of these communities, may change with time or circumstance, and may not be binding. Consequently, the Committee considers that the social and moral concerns raised by embryo research and human cloning may not be explained simply by reference to a single set of values, beliefs and interests (or 'standards') held by a single 'community'.

The need to take account of community standards was therefore a challenging requirement for the Committee. As described in Chapter 3, the Committee gathered information from the general public and those with a specific interest in the issues involved through a call for public submissions and a range of public and private hearings, site visits and discussion forums. While these submissions and meetings provided information relating to different interests and perspectives within the community, they could not be considered to represent a quantitative survey of community standards. For quantitative information, the Committee had access to the results of a survey by the Biotechnology Australia Public Awareness Program (see Section 7.3).

This chapter provides an overview of the issues raised in the submissions and hearings and provides a short summary of the findings of the Biotechnology Australia survey. The focus of the chapter is on the overarching issues associated with the definition, social and moral status of a human embryo, the acceptability of creating and using human embryos for research and to derive therapeutic products, and the social and moral obligation to provide benefit to people who are ill. It is important to realise that other social and ethical issues were raised, such as the role of women in providing oocytes for nuclear transfer, consent for donation of embryos, and commercialisation of reproductive products and human embryonic stem cell lines. These are discussed in chapters relevant to those issues.

7.2 Submissions and hearings

The moral status of the human embryo was an important theme of the submissions and hearings. Many respondents stated that any research on human embryos is unacceptable, while many others argued that the potential benefits of research on a human embryo at the earliest stages of its development outside a woman's body justify such use.

The submissions and hearings highlighted the importance of clearly defining the term 'human embryo', and clarifying whether people were talking about the same things. The biological definitions of 'human embryo' and 'human embryo clone' are discussed in Chapter 8. Social and moral aspects are considered in this section.

Social and moral definitions of 'human embryo'

Dr Sheryl de Lacey, a reproductive health researcher, suggested that legislation should take account of cultural understandings of an embryo:

> The current definition of an embryo is very scientific, which is valid but does not relate to peoples' understanding about things such as genetic connectedness, kinship, physical/ emotional effort in production, potential child and family tree.
> *Dr Sheryl de Lacey, Research Centre for Reproductive Health, University of Adelaide (Adelaide hearings)*

This concept was a recurring theme in many submissions and at the hearings. Within this discussion, several themes emerged:

- the intended use of the embryos (eg for implantation into a woman or for research)
- the way the embryo was created (fertilisation versus other means)
- the social relationships of the embryo (for example, as part of a family with 'parents', a family tree and so on)
- the status of the embryo in terms of its potential for human life (and the respect this should be accorded) versus the potential for research to benefit people.

The intended use of the embryo

Many respondents both at the hearings and in the submissions referred to how the intended use of embryos affected their perception of them.

> Need to rethink current overly broad use of term 'embryo'. Most community understanding involves penetration of egg by a sperm and involvement of sexual reproduction contributes to the moral significance. Whether sexual reproduction is involved in the cell's creation, as well as whether it is intended to be part of a parenting project — contribute to moral status. A dividing cell created by SCNT is importantly different because of the intentions of those forming it. *Dr Leslie Cannold, Centre for Applied Philosophy and Public Ethics, University of Melbourne (Melbourne hearings)*

> There is nothing in the definition that distinguishes a human cell that is capable of some type of development … and those which are orientated towards resulting in a child being born.
> *Queensland Right to Life (Submission LRC376)*

Speaking at the Melbourne hearings, Professor Louis Waller, Monash Law, Monash University, told the Committee that the focus in Victoria in the 1990s was on intention and that this was well understood as follows:

> If the intention was to form those embryos for the purposes of IVF (ie to create a child), it was permissible. If, from the outset, the intention was to form those embryos for the purposes of destructive experimentation, it was not permissible. Embryos that were formed with the intention of transfer but for one reason or another were not transferred, embryos which, in fact, might be untransferable because of their condition so that no responsible doctor would undertake that procedure, might very properly be used for experiments, particularly when those experiments were intended to improve the very processes with which we were concerned.
> *Professor Louis Waller, Monash Law, Monash University (Melbourne hearings)*

This is also the current position of the RIHE Act. However, Professor Waller also noted that, as the intention of embryo research is to benefit people with serious diseases, this outcome (ie treatment of disease) should be taken into account in the same way as the outcome of creation of a child (ie treatment of infertility). At the Brisbane hearings, Associate Professor Malcolm Parker took this argument further:

> But I would suggest that the IVF procedures which produce embryos which are subsequently destroyed are no morally different from the cloning procedures which would do the same thing … Therefore, under the current arrangements — the implication is that it is more important/OK to benefit people with a 'child wish' than to benefit people with a 'health wish' (as both involve creation and destruction of embryos but one is allowed while the other is banned). *Associate Professor Malcolm Parker, School of Medicine, University of Queensland (Brisbane hearings)*

Professor Louis Waller referred to the term 'pre-embryo' to distinguish an embryo that is not destined to create a child, and noted that this term had gained some acceptance elsewhere. However, others cautioned about the dangers of making biological definitions do moral work:

> In view of the current debate over the creation and use of human embryos, the definition of an embryo needs to be in terms of what an embryo is, not in terms of the various purposes that scientists might have. *Father Gerald Gleeson, Catholic Institute of Sydney (Submission LRC379)*

> I think that would be a case of persuasive redefinition. I think an embryo is basically a human life form with the capacity to produce an entire human being if placed in a woman's uterus. That embryo may have two different kinds of moral status. It may have a very high moral status when it's placed in a uterus of a woman who wants to have that child, especially when it's a part of a parental project. It has a lower moral status when it's not a part of that parental project. *Professor Julian Savulescu, Director, Oxford Uehiro Centre for Practical Ethics, University of Oxford (Sydney hearings)*

> … what I think is important, particularly with regard to the human embryo, is to call embryos embryos … and then start to distinguish underneath the ways in which they're created, the potentials that they have and the intentions for which they've been created. And all of those things I think are different. That doesn't mean some of them aren't embryos and some of them are. What it does mean though is our moral distinctions between what we should be allowed to do with those will differ … That doesn't change the fact however that the overarching definition is embryo. *Dr Rachel Ankeny, University of Sydney (Sydney hearings)*

Method of creation

Some respondents distinguished between an embryo formed by the fusion of a sperm and egg and one formed by alternative means: the former having the social significance of being formed within the context of a family unit; the latter not having that significance, but rather being the product of research, suitable for research or therapeutic uses:

> Consideration of any moral difference between an SCNT embryo and a 'natural' embryo may help to 'unpack' different ways of creating an embryo (fertilisation versus SCNT). For example, it would be valuable to separate out whether the important difference is because of the way the different embryos are formed or because of the intended use.
> *Associate Professor Wendy Rogers, Department of Medical Education, Flinders University (Adelaide hearings)*

Professor Simon Carroll (AusBiotech) suggested that there needs to be a separate term for the entity formed by fertilisation from a cellular mass that has been derived by nuclear transfer and may give rise to a therapeutic potential. He suggested the word 'progenitor' for the latter situation. Other scientists did not agree that such a distinction is necessary:

> The term 'human embryo clone' is ambiguous … The current terminology may lead to the mistaken belief that the intended use of the 'human embryo clone' is only to create a 'cloned' human … The term 'human nuclear transfer embryo' is more appropriate as it clearly and unambiguously states the method of derivation. *Stem Cell Sciences Ltd (Submission LRC318)*

Other respondents also regarded an activated nuclear transfer embryo as different from an embryo formed by fertilisation:

> If the law said that the SCNT embryos cannot be implanted, then they would not be a potential human being but 'just a bunch of cells'. As long as you don't see that embryo as going forward to forming an organism, this is better than destroying an embryo that was created as a new life. *Associate Professor Melissa Little, Institute for Molecular Bioscience, University of Queensland (Brisbane hearings)*

> Defining SCNT as an embryo is not useful. Current definition alludes to the cell's past as well as its future potential. But the cell formed from nuclear transfer is different from one formed from fertilisation (intent is different, use is different) … People have an idea of what an embryo is. SCNT doesn't have the same characteristics … Need to use the most descriptively clear terms possible in order to advance an honest and accurate understanding amongst the public of

> the issues involved. *Dr Leslie Cannold, Centre for Applied Philosophy and Public Ethics, University of Melbourne (Melbourne hearings)*

The Australian Academy of Science combined the scientific rationale of pluripotency with method of creation (fertilisation versus nuclear transfer) and intention for use (fertility treatment versus research or cellular therapies) to argue for different definitional classes of embryos:

> Cells that are studied entirely in vitro in a research context, and are not formed from a fertilised embryo, should not be regarded as embryos … This includes pluripotent cells derived by nuclear transfer. *Australian Academy of Science (Submission LRC18)*

The submission from Stem Cell Sciences Ltd expressed a compromise position — that a nuclear transfer embryo is potentially the same as an ART embryo but, if this potential is not realised (by implantation into a woman), it can be considered differently (as a source of cells for research or therapy):

> The resulting 'human nuclear transfer embryo', while likely to have a poor likelihood of successful implantation and development to term if transferred to the body of a woman, should be considered as potentially equivalent to a normal ART embryo and its use for reproductive purposes prohibited as stipulated in the existing *Prohibition of Human Cloning Act 2002*. However, if the nuclear transfer embryo remains in the laboratory, pluripotent stem cells could be isolated for research. *Stem Cell Sciences Ltd (Submission LRC318)*

Putting this another way, this means that it is the act of implantation into a woman that should be prohibited rather than the technology itself:

> Both 'reproductive' cloning and so-called 'therapeutic' cloning involve the use of … SCNT … Where 'reproductive' and 'therapeutic' cloning deviate is in how the resulting 'nuclear transfer' embryo is treated. It either remains in the laboratory in the case of 'therapeutic' cloning' … or the resulting 'nuclear transfer' embryo is transferred to a woman. It is the act of transferring the embryo, not the act of creating the embryo that should be prohibited. *Stem Cell Sciences Ltd (Submission LRC318)*

Others did not agree with this position. However, most agreed that human embryos should not be used for research purposes or developed outside the body of a woman beyond the stage when implantation would have occurred (approximately 14 days from conception).

Social relationships

Several respondents stressed that an important aspect of defining an embryo was the relationship between the embryo (however created), its immediate genetic 'ancestors' and the broader community:

> … the current legislation defines the embryo purely in terms of its genetic constitution and that as I've said already implies … an impoverished view of human life … But … we understand that the human being is fundamentally one who is involved and defined … within a web of relationships … At conception we are enmeshed in a whole web of relationships immediately so that we would understand that no human being at any stage can be treated as an instrument in any way at all. *Reverend Ross Carter, Bioethics Committee of the Uniting Church in Australia, Synod of Victoria (Melbourne hearings)*

> Does not think that the name 'embryo' is the most important thing to most people. Most important thing is what it means to them. *Dr Sheryl de Lacey, Research Centre for Reproductive Health, University of Adelaide (Adelaide hearings)*

Within the context of ART services, embryos have a clear social value for the couples who have created them, who regard them as their potential children:

> They see it more within their family tree … So they see it as a potential child and as a potential child of theirs, should it come into being. *Dr Sheryl de Lacey, Research Centre for Reproductive Health, University of Adelaide (Adelaide hearings)*

Some consumers of IVF stressed that, while their embryos had a very real status as a potential child within their family, when they had reached the decision that they had completed their family, donating their spare embryos to research was further acknowledgment of their value and therefore preferable to discarding them.

> Some offensive things have been said about how infertile people treat their stored embryos. IVF couples care very much about the fate of their embryos. [They value] life and children. Opportunity to donate to research or to another couple gives them some meaning.
> *Ms Sandra Dill, Executive Director of ACCESS (Australia's National Infertility Network) (Sydney hearings)*

Some respondents felt that the family connections of embryos formed by fertilisation for ART treatment are what defines them as potential human beings. Embryos created by SCNT purely for research do not have this social connection and are therefore not (in social terms) potential human beings.

> ACCESS supports the use of SCNT … These embryos are fundamentally different from other embryos, as they are not created with human sperm.
> *ACCESS (Australia's National Infertility Network) (Submission LRC899)*

> ... cells created by somatic cell nuclear transfer for the purpose of creating patient specific stem cells necessary to save that patient's health or life is importantly different from a one celled embryo created by a sexual or reproduction [sic] either in a dish during IVF treatment or in a woman's body during intentional sexual reproduction both because of the way in which the embryo was formed and the intentions of that format. *Dr Leslie Cannold, Centre for Applied Philosophy and Public Ethics, University of Melbourne (Melbourne hearings)*

Some took this further and submitted that an embryo formed by SCNT is an extension of the person from whom the somatic cell has been taken:

> Perhaps most importantly, cloned embryonic stem cells allow us to generate populations of stem cells which are genetically identical ... If a consenting adult donates a cell to research, we should have a similar respect for this person's desire that their tissue should be used to help identify more effective treatments for other human beings. *Professor Julian Savulescu, Director, Oxford Uehiro Centre for Practical Ethics, University of Oxford, and Mr Bennett Foddy, Ethics Unit, Murdoch Children's Research Institute (Submission LRC601)*

> Cells that are studied entirely *in vitro* in a research context, and are not formed from a fertilised embryo, should not be regarded as embryos. They are cell lines containing the diploid genome of a living person, grown in a laboratory. This includes pluripotent cells derived by nuclear transfer. *Australian Academy of Science (Submission LRC18)*

Others did not agree:

> Embryos do not have to have male and female genetic material, the main criterion is that they can develop into a person (and have human ancestors etc). We don't regard an identical twin as merely an extension of the other person. *Most Reverend Professor Anthony Fisher, Catholic Archdiocese of Sydney (Sydney hearings)*

Status of a human embryo

Discussions about the use of embryos in research inevitably revolved around the status of the embryo as a human being at different stages of its development. A report published in March 2005 by the United Kingdom House of Commons Science and Technology Committee, *Human Reproductive Technologies and the Law: Fifth Report of Session 2004–05,*[22] states three fundamental principles that underpin discussions of the status accorded to a human embryo:

> (a) that the embryo is human life and therefore is entitled to conferral of full human rights;

22. See http://www.parliament.uk/index.cfm

> (b) that the development of personhood is a gradual process but that the embryo is entitled to some protection; and
>
> (c) that the embryo is no more than a collection of cells, albeit with the potential to develop into a human being.

These three positions were all expressed in the hearings and submissions. While position (a) was more likely to be expressed by community and religious groups and position (c) was more likely to be expressed by scientists, this was not universally the case, and differences of opinion were evident within every professional and social group that came to the table:

> There are different opinions within the Christian church (and over time). Some people within the church think that implantation is the point of personhood — there is diversity in the church and the churches tradition. *Reverend Ross Carter, Bioethics Committee of the Uniting Church in Australia, Synod of Victoria (Melbourne hearings)*

Some said that, from the outset, an embryo is an individual person:

> The great failure of the definition of 'human embryo' is to omit that: From and including the zygote stage the human embryo, throughout the whole utero development period, is a complete and distinct human person, a human being, with full human rights and dignity of life necessarily accorded him, or her.
> *Mr Gerard Calilhanna, New South Wales (Submission LRC254)*

The Christian Democratic Party (Western Australian Branch) argued that:

> … a human embryo is a living human organism with unique adult characteristics already determined. Though not yet expressed, individuality is inherent and real in the genetic programming from the time of fertilisation. *Christian Democratic Party, Western Australian Branch (Submission LRC373)*

Others acknowledged an embryo as being human (ie having a human genome) but not as being an individual human being:

> Embryos definitely have potential to become humans — but not by themselves, and not without medical intervention. They most definitely don't have any of the functions, awareness and identities we associate with humans and as brutal as it may sound, are 'only' a group of cells that will remain just as that, unless they are planted into the womb of a woman.
> *Mr Taito Peura, New South Wales (Submission LRC458)*

> Personal definition of an embryo is the beginning of a potential life. A blastula is not a potential life (seed to a plant) until point of implantation. *Associate Professor Melissa Little, Institute for Molecular Bioscience, University of Queensland (Brisbane hearings)*

The Committee also heard that the nature of 'personhood' is an extremely problematic area of philosophy overall, and is particularly so in relation to the embryo:

> … the definitions are unclear as to when a clump of cells becomes a real person. I favour the 'potential' understanding where the DNA present can potentially deliver a human outcome — that determines personhood. *Reverend Graham Castle, New South Wales (Submission LRC548)*

> But for those with a religious background there still is the whole question of what constitutes early human life as opposed to cellular life and even if you believe that early cellular life is potential human life are you ever justified in work or research that may lead to the destruction of it? My own view is … that the fertilised mass of cells to the blastocyst stage is so undifferentiated, and really almost up until 14 days with the beginning of the primitive streak we are justified in observation at least and careful observation and at the earliest stage before the cells have moved very far, we possibly are justified in carrying out work which may lead to their destruction. But it's not a destruction which you pursue mindlessly … In other words an ethic of care and responsibility. *Professor John Morgan, Director of the Australian Institute of Ethics and the Professions, St John's College, University of Queensland (Brisbane hearings)*

Those who held the view that an embryo is not a unique person from conception tended to support regulated research on embryos at early developmental stages (usually up to 14 days post-fertilisation):

> [Recommendation] Declare at law that a blastocyst is not human and, that research involving somatic cell nuclear transfer may be lawfully conducted on embryos which are 14 days old or below. *Mr Adam Johnston, New South Wales (Submission LRC287)*

> We believe the current definition of 'human embryo' and its legal treatment in the Act fail to draw a reasonable distinction between the early and late embryo. It is debateable whether the human conceptus in the first 14 days of its development should be considered an embryo at all. The UK does not grant the embryo any legal protection until the formation of the primitive streak, 14 days into development. The Australian government should consider following the UK's example. *Third-year Bachelor of Biomedical Science students, University of Melbourne (Submission LRC449)*

Some participants stressed that there is no intrinsic moral difference for different intended uses, as the potential of the embryos remains the same in each case:

> Some may say that if an embryo is going to be discarded, it has less value than one to be implanted. This is not the *intrinsic* value as such but the valuation by parents. In terms of potential, there is no difference between them … However, a different moral significance may be attributed according to the intended use of the embryo (eg the potential as a human being may be seen as more morally weighty than potential for research to benefit people; or the reverse). *Associate Professor Malcolm Parker, School of Medicine, University of Queensland (Brisbane hearings)*

The concept of an embryo's potential and ability to direct its own development was captured in a suggested definition of human embryo provided by Associate Professor Bernadette Tobin:

> … any cell or organism, however formed, that may be distinguished from ordinary cells by having a potential to develop in an integrated way towards forming a foetus, similar to the potential of the cell formed by the fusion of an ovum and a sperm. *Associate Professor Bernadette Tobin, Director, Plunkett Centre for Ethics, Australian Catholic University (Submission LRC550)*

Many of the respondents who assigned personhood to an embryo from the moment of conception did not distinguish between a human embryo created by fertilisation and a human embryo clone. For example:

> [Similar to the definition of 'human embryo'] the definition of 'human embryo clone' needs to acknowledge that the human clone is also a distinct human. However, the definition of a human embryo clone must not in itself indicate that permission to create a human embryo clone is inevitable or desired. *Mr Gerard Calilhanna, New South Wales (Submission LRC254)*

> Contra to the statement in the Issues Paper, 'a human embryo clone is a human embryo … ' a human embryo *is* a human being … A human embryo does not *become* a human being because it *is* a human from the time of fertilisation … *Right to Life Australia (Submission LRC288)*

At its informal meetings with a representative of the Northern Land Council and the Aboriginal Medical Services Alliance in Darwin, the Committee heard that the diversity of Indigenous views relating to the issues covered by the Acts was likely to be as large as those expressed by other sections of society, and include personal, religious, cultural and spiritual beliefs. However, there has been very little discussion of the issues covered by the Acts among Aboriginal and Torres Strait Islander communities and little opportunity to bring an Indigenous sense of ethics to the discussions. Overall, however, there is deep suspicion of such medical technologies among Indigenous communities.

Use of human excess ART embryos in research

Definition of 'excess ART embryo'

Some people expressed concerns about the definition of an 'excess ART embryo'. For example, one submission expressed concern that the consent arrangements for determining an embryo to be an excess ART embryo are not clear (Confidential submission LRC477).

Associate Professor Bernadette Tobin thought that the definition had been clear while the sunset clause was in place restricting the use of embryos to those created before 5 April 2002 (see below). However, since the clause has been lifted, embryos can be used almost immediately, and it is therefore no longer clear if they are genuinely 'excess':

> … there's an ambiguity in the definition of an excess IVF embryo … now because of the time passing, with the confinement of damaging or destructive uses of embryos to those created before the 5th April 2002, now that that's lapsed we've got a new situation in which embryos can be formed and found to be not suitable for implantation or not desirable for implantation … They become excess IVF embryos immediately and it seems to me that that wasn't what the legislators had in mind. They meant genuinely surplus at the end of your treatment and I think that that ambiguity needs to be cleared up and I think that … either the Act … or the guidelines need to be amended to make sure that the embryos that become available for destructive research are those that are found to be genuinely surplus only after the woman and her spouse have made a decision not to continue with ART treatment. *Associate Professor Bernadette Tobin, Director, Plunkett Centre for Ethics, Australian Catholic University (Sydney hearings)*

However, others felt that there are no grounds for this concern as the legislation requires embryos to be first declared excess. They may then, in a separate process requiring 'proper consent', be donated to research. 'Proper consent' (according to the ART Guidelines 2004) includes a two-week cooling-off period between giving the consent and the research taking place. Further information about consent is in Chapter 11.

Numbers of excess ART embryos

The existence of large numbers of excess ART embryos continued to be a matter of serious concern for some people:

> The use of 'spare' embryos for secondary purposes will inevitably create a demand for the production of more and more 'excess' embryos to supply such unacceptable secondary purposes. *Mr Gerard Flood, Victoria (Submission LRC395)*

At the Sydney hearings, Reverend Dr Norman Ford and Mr Michael Herbert, representing the Caroline Chisholm Centre for Health Ethics Inc, were also concerned that far more embryos are created than are needed. They suggested that this should be monitored so that the number created is only sufficient for fertility purposes:

> The number of embryos created for the purposes of achieving a pregnancy needs to be monitored. It should be illegal to create more embryos than is realistically needed in order to guarantee a supply of spare embryos. The law against creating human embryos for research should not be allowed to be flouted in this way.
> *Caroline Chisholm Centre for Health Ethics Inc (Submission LRC392)*

Asked about this issue at the Hobart hearings, Dr Bill Watkins, Director, Tasmania IVF, explained that:

> … we like to get as many embryos as we can … but that's without over stimulating their ovaries. We don't push the dose hoping to get a lot of eggs. We aim for ideally 10 or 12 eggs … So as a result you might get 6 embryos out of 10 or 12 eggs … You'll always have the problem of excess embryos … But we also ask our patients how many embryos or how many eggs they want to fertilise and we have a small percentage of patients electing to only try and fertilise 6 eggs because they don't want to have that issue of embryos left over at the end of the day. But that's not a perfect solution … a perfect solution would be to freeze the eggs and only pull them out of the freezer and fertilise them when we need them. But until we can get much, much better at that we'll have to go on making embryos. *Dr Bill Watkins, Director, Tasmania IVF (Hobart hearings)*

As ART is regulated by the Reproductive Technology Accreditation Committee (RTAC) under the RTAC Code 2005, monitoring of the number of embryos created is already occurring (and has been since before the legislation was passed in 2002). Accredited ART clinics are required to submit the numbers of embryos created in each cycle, and the numbers used, stored and so on, to the National Perinatal Statistics Unit of the Fertility Society of Australia, and these figures are publicly available.[23] State reproductive technology agencies also maintain records for their own states. For example, the Western Australian Reproductive Technology Council told the reviews that it monitors the creation and storage of embryos in Western Australia.

Use of excess ART embryos for research

Most scientists and many other organisations and individuals supported the use of excess embryos for destructive research, both for ART research and also to obtain embryonic stem cells:

> The Australian Society for Medical Research supports … a continuation of the 2002 legislation authorising the destruction of human embryos including derivation and studies of embryonic stem cells. *Australian Society for Medical Research (Submission LRC245)*

> I support the regulated use of excess ART embryos for the creation of new human embryonic stem cell lines and for the creation of SCNT-hESC lines. *Mr Justin Lees, Diabetes Transplant Unit, Prince of Wales Hospital, Sydney (Submission LRC441)*

> I support both adult and embryonic stem cell research using excess IVF embryos. *Mrs Rosemary Langford, New South Wales (Submission LRC456)*

> [Recommend] that the use of surplus embryos be permitted in Stem Cell Research where such embryos resulted from attempts to obtain a pregnancy by means of Assisted Reproductive Technology and where the biological parents of embryos wish to donate them for such research. *Stem Cell Ethics Australia (Submission LRC396)*

> The Research Involving Human Embryos Bill 2002 enables the production of new hES cell lines under careful regulatory guidelines. The ability to generate new hES cell lines is critical to progress in this field, and Australian scientists should participate in the international effort to derive new cell lines with improved properties using new technologies. Implementation of the provisions of the Sunset Clause of this Bill will ensure that Australian researchers can continue to play an active and leading role in this important activity. *Dr Martin Pera and others, Monash University (Submission LRC509)*

> On behalf of our members with diabetes, we recommend that any legislation referring to human embryonic research be sufficiently comprehensive to allow for unwanted and/or discarded embryonic tissue to be made available for stem cell research. *Diabetes Australia — New South Wales (Submission LRC536)*

> … existing legislation should continue to support the derivation of new embryonic stem cell lines from the donated human embryos … we don't want to open up again this issue and we don't want to open up the so-called moral debate again to go backward … the progress in the field of human embryonic stem cell research has been phenomenal throughout the world and more so in Australia … We want to maintain that lead … I think it is a record in the scientific world that more has been published about human embryonic stem cell research in the top class journals like *Nature* and *Science* during the past 4 to 5 years than in any other field to the best of my knowledge and that adds credibility to this research and that proves the scientific legitimacy of what is being done on human embryonic stem cell research. *Dr Kuldip Sidhu, Chief Hospital Scientist, Diabetes Transplant Unit, Prince of Wales Hospital, Sydney (Sydney hearings)*

Others did not think that this practice should be allowed to continue:

> We oppose the use of 'excess' embryos for any purpose other than implantation into the uterus of a prospective mother or a prospective adoptive mother. *Christian Democratic Party, Western Australian Branch (Submission LRC373)*

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23. National Perinatal Statistics Unit, Assisted reproductive technology series, 1993–2004 http://www.npsu.unsw.edu.au/Publications.htm#ART

> … as an ART user myself … I do not know how this technology was developed, but it most certainly does not need to be further developed at the expense of precious human lives in embryonic form. Let us be a nation that respects life, especially life in its most vulnerable state. *Mrs Rachel Jenner (Submission LRC464)*

> We are, and always have been opposed to the use of 'excess' human embryos from the ART programme. It is inconsistent with the dignity belonging to human beings to freeze them, call them 'excess' as if they were an assembly line product, and use them for destructive purposes. Since they are not destined for implantation, anything done to them will necessarily not be for their benefit. We are opposed to any extension of the license to use embryos created after 5th April 2002. *Queensland Right to Life (Submission LRC376)*

At the Melbourne hearings, Reverend Ross Carter and Dr Rosalie Hudson of the Uniting Church further noted that, although production of embryos for reproduction may require that they are destroyed after a certain period of time, there is a strong distinction between allowing an embryo to succumb and using it as a product.

In Western Australia, under the *Human Reproductive Technology Act 1991* (WA HRT Act), the Western Australian Reproductive Technology Council's approval is required to carry out a diagnostic procedure on an embryo unsuitable for transfer. Also, although the WA HRT Act (like the RIHE Act) only regulates the use of embryos that are live, the council ensures that any consent given for any subsequent use of nonviable embryos is done so freely and is well informed. The use of nonviable embryos for preimplantation genetic diagnosis training has now been approved in three clinics (Confidential submission LRC410, quoted with permission of the author).

See Section 8.2 for further discussion of 'live' and 'viable' embryos.

Decision making about the use of excess embryos

Those most affected by the decision about whether to use human embryos for research, the users of ART services, noted that making the decision about what to do with their excess ART embryos was distressing. However, many preferred their embryos to be used for research than to be 'wasted':

> I've spoken with a number of people who would be interested in donating their embryos to stem cell research for their own family benefit so that they are talking more about their desire to have HLA matched material … I've spoken with 28 people so far who have donated embryos to research and every single one of them has said to me that they did that because they didn't want their embryos to be wasted. *Dr Sheryl de Lacey, Research Centre for Reproductive Health, University of Adelaide (Adelaide hearings)*

> For many couples, the opportunity to donate their embryos for ART research gives them some added meaning, as they contribute to scientific knowledge that will lead to improvements in ART practice and ease human suffering. *ACCESS (Australia's National Infertility Network) (Submission LRC899)*

This position was also supported by research on decision making by ART couples:

> The study found that most couples (58%) preferred embryos to come to some use, rather than being disposed of. Almost half the sample reported finding the decision making to be distressing. A majority approved of embryo donation for stem cell research
> [From 'Deciding the fate of supernumerary frozen embryos: A survey of couples' decisions and the factors influencing their choice', a study by Karin Hammarberg and Leesa Tinney; Monash IVF and University of Melbourne, *described in Submission LRC306 and quoted with permission of the authors*]

(See Section 11.2 for further information on consent for donation of excess ART embryos for research.)

At the Brisbane hearings, Dr Keith Harrison, Scientific Director, Queensland Fertility Group, told the Committee that before 2002 approximately 90% of couples asked for their excess embryos to succumb, only a few donated them to research, and a few donated to other couples for ART. After stem cell issues

were highlighted in the media, large numbers started to donate their excess embryos for research (the proportion rose from about 10% to about 20%). However, Dr Harrison did not think that ART consumers make a distinction between ART research and stem cell research; rather, they just want some good to come from their embryos.

Similarly, at the Melbourne hearings, Dr John McBain, Director, Melbourne IVF, reported that at the end of the storage period approximately 5–7% choose to donate to another infertile couple (this proportion has not changed since the introduction of legislation), but the proportion who donate for research has dramatically increased (he estimated that this is now close to 60%). In response to a question about how many of the embryos were donated for ART research and how many for stem cell research, Dr McBain said that he did not know — but most media coverage has been about stem cell research.

Dr Keith Harrison told the Committee that the Queensland Fertility Group has a large number of embryos in the freezer that have been donated in principle for research but that have not been allocated to a specific research project. The clinics no longer accept further embryos for research because they cannot see any use for them. The same point was made at the Adelaide hearings by representatives of the South Australian Department of Health and South Australian Council on Reproductive Technology, who noted that in South Australia many couples have completed the first stage of donating their excess embryos in principle to research. These embryos are held at each clinic awaiting suitable research opportunities at that clinic. However, there are currently no licensed embryo research projects in South Australia, and therefore no embryos have been used. These representatives suggested that it may therefore be worthwhile considering the establishment of an 'embryo bank', or register of excess ART embryos (that is, a list of excess ART embryos available for research and the clinics holding them) so that researchers from other institutions can access them.

Other organisations also agreed that the couples responsible for the embryos should be able to decide whether they can be used for research:

> Representing patient groups, we believe that it should be the choice of the parents to decide whether they wish their excess IVF embryos discarded, or whether to allow them to potentially save the lives and improve the quality of life of others less fortunate … Allowing individuals this choice provides them the opportunity to make their own moral decisions. *Spinal Cure Australia (Submission LRC308)*

Some respondents favoured adoption as a better option for the use of excess embryos.

> More embryos would be given the opportunity of life (and thus made more accessible) if embryo adoption was promoted more. *Mrs Rachel Jenner (Submission LRC464)*

> With regard to the so-called 'spare' embryos produced in IVF we believe there are two possibilities. (1) Donation of embryos to childless couples for who even IVF has not worked … (2) The embryos should be allowed to die, or to succumb. *Reverend Ross Carter and Dr Rosalie Hudson, Bioethics Committee of the Uniting Church in Australia, Synod of Victoria (Submission LRC486)*

Several respondents to the submissions, attendees at the hearings and participants in the discussion forums expressed surprise to find that of the nine licences granted so far, only four were for extraction of embryonic stem cells. The other five were for ART research. These participants felt that there had not been any public debate about the use of embryos for ART research, as all the publicity in 2002 was about stem cell research:

> … for only 150 out of the 1735 human embryos for which licenses have been issued is stem cell therapy mentioned as a justification … There is as yet no proof from animal models that embryonic stem cells can be used for safe, effective therapies for either Parkinson's, juvenile diabetes or any other condition. Until this is established then no approvals for research involving human embryos based on claims that stem cell lines derived from these human embryos will be used for therapies should be granted.
> *National Civic Council (Submission LRC246)*

Creating human embryos for research or development of therapeutic products

Discussions about the status of human embryos were closely related to discussions about the acceptability of creating embryos specifically for research. The views expressed related mainly to the two positions highlighted in the Issues Paper:

- *Against:* As a human embryo clone is a human embryo (capable of becoming a human being), it is wrong to create one specifically to destroy it. Adult stem cells show potential for development of stem cell therapies that is similar to that of embryonic stem cells and their use does not involve the destruction of human embryos.
- *For:* It is acceptable to create and use preimplantation human embryos for research that may benefit human health and wellbeing by development of stem cell therapies to repair damaged and diseased tissues. It is not known at this stage whether embryonic or adult stem cell research will provide greater benefits (if any), so it is legitimate to progress both pathways until a clearer picture emerges. (See Appendix 2 for a copy of the Issues Paper; a discussion of embryonic stem cell and adult stem cell research is in Chapter 5).

At the Adelaide hearings, Dr Peter Woolcock, Deputy Chair, South Australian Council on Reproductive Technology, noted that some people may be adopting a third position by inference:

> It's a serious matter to destroy an embryo but it only should take place when a greater benefit will result. *Dr Peter Woolcock, representing South Australian Council on Reproductive Technology (Adelaide hearings)*

Examples of comments against creating embryos for research or development of therapies included:

> The deliberate creation of a human being, with the intent of killing it for a particular organ later down the track is murder. *Ms Cheryl Clough (Submission LRC612)*

> There is no … consensus [of Stem Cell Ethics Australia] in support of the view that new embryos should be able to be created for the specific purpose of research.
> *Stem Cell Ethics Australia (Submission LRC396)*

The Victorian Government also stated that:

> The creation of ART embryos specifically for research should continue to be prohibited.
> *Victorian Government (Submission LRC537)*

Arguments put forward in support of the creation of embryos for research purposes included:

> … opponents of therapeutic cloning often rely on the argument that it is less morally serious to use spare IVF embryos in research than to create and destroy embryos specifically for research. This argument cannot be sustained … In both cases, embryos are created and destroyed in pursuit of human welfare … Both kinds of embryos have the potential to develop into a person, so a moral distinction between them cannot be grounded on potentiality … Furthermore, a moral distinction can not be made on the basis that spare IVF embryos had a chance of becoming a person, whereas those created expressly for research never did, and that this constitutes greater instrumentalisation and exploitation of these embryos. *Associate Professor Malcolm Parker, School of Medicine, University of Queensland (Submission LRC311)*

> If there is no right to life/preservation attaching to an early embryo, then no related moral justification is needed regarding the creation of embryos for research. *The only justifications needed here would be prudential*: relating to the scientific point of research; and this is not a matter for legislators … there is no compelling reason, morally or legally, to reject the deliberate creation of human embryos for research.
> *Dr Michael Carey, University of Technology, Sydney (Submission LRC784)*

Dr John McBain (Director, Melbourne IVF), representatives of Sydney IVF, Professor HW Gordon Baker (ART researcher, Victoria) and others told the Committee that fertilisation of an egg by a sperm would be a helpful procedure to improve ART clinical practice (see Section 4.3).

A submission from 75 third-year Bachelor of Biomedical Science students at the University of Melbourne also believed that the creation of embryos for research should be permitted:

> We oppose Section 14 of the Act, as we believe that researchers ought to be permitted to create embryos for the purpose of research (with the informed consent of responsible persons involved in donation of the egg and sperm) rather than being restricted to using excess assisted reproductive technology embryos. It is difficult to see how an embryo created and destroyed for research purposes can be considered to have been harmed; it is in no worse a position than if it had not been brought into existence in the first place. *Third-year Bachelor of Biomedical Science students, University of Melbourne (Submission LRC449)*

However, the Australian Academy of Science recommended that the ban on creating embryos using egg and sperm for research purposes should remain. When asked at the Melbourne hearings why the Academy had taken this position, Professor Bob Williamson said that:

> … we were unable to come up with any situation where the creation of an embryo deliberately from an egg or a sperm for research purposes was necessary in order to answer a scientific question. *Professor Bob Williamson, representing the Australian Academy of Science (Melbourne hearings)*

He further added that it might be possible to use this method to study some single-gene disorders (as every embryo produced would have this gene). However, most of the diseases of interest in this field of research are multifactoral, and in such cases SCNT is a much better method to get a genetic replica of an individual.

When asked how he would respond if there were a scientific reason to create an embryo from egg and sperm (ie to isolate the moral basis from the scientific basis for the recommendation), Professor Williamson said (speaking personally) that there is a view in society that creating embryos for research is unacceptable and he did not see a major benefit to people for creating an embryo in this way.

As described in Section 6.3, many arguments were presented both for and against creating embryos by nuclear transfer or other related methods to generate patient-matched stem cells (‘therapeutic cloning’).

Many of the written submissions received were from individuals suffering from disease, or individuals who know someone else with disease. The diseases described included diabetes, spinal injury, Parkinson’s disease and motor neurone disease. Almost all of these submissions saw embryonic stem cell research as a major source of hope of a cure for their disease:

> As a type one diabetic I see one of the few avenues for a cure for my condition being research, which should be allowed to access embryos if required in order to better understand the condition its causes and potential cures. Many millions of people around the world have T1D, and many cope quite well, with this disease, however many struggle daily with it and several friends of mine have committed suicide as a result of it and their perception that there is no cure in sight, please do not block the light at the end of the tunnel.
> *Mr Matthew Beecroft, Victoria (Submission LRC329)*

However, others did not support human cloning for research purposes, such as an individual with spinal injury:

> As a quadriplegic, I would love to see a cure for my problem, and other medical conditions, but never at the cost of another human life … *Ms Joy Hockings (Submission LRC56)*

The Coalition for the Advancement for Medical Research in Australia (CAMRA) (an organisation representing people with disease and disability) supported human cloning for research:

> … therapeutic cloning (Somatic Cell Nuclear Transfer) or ‘patient specific stem cell’ research is NOT reproductive cloning. It has the potential to address major diseases for individuals their families and the broader community … The possibility of a cure — no matter how remote — is critically important. *CAMRA (Submission LRC17)*

However, at the Perth hearings, Dr Peter Williamson, an academic suffering from Parkinson's disease, commented that the Parkinson's Association of Australia did not put in a submission to the review, which may have been because there was some concern about raising false hopes for sufferers. Nevertheless, Dr Williamson stated:

> I looked at it fairly objectively and I think from my knowledge of science and reproduction that there are certainly going to be benefits ... But, as I say, the timeframe won't catch me — I'm probably going to miss it, but there are going to be a lot of people who do benefit from this form of research in future. *Dr Peter Williamson, Western Australia (Perth hearings)*

7.3 Biotechnology Australia survey

Biotechnology Australia is the Australian Government agency responsible for managing the national Biotechnology Strategy. It has commissioned regular research as part of its work to understand and track public understanding of and attitudes towards advances in biotechnology.

Market Attitude Research Services Pty Ltd was commissioned by Biotechnology Australia to examine Australian community public opinion, knowledge and understanding relating to human stem cell research and associated issues every year since 2002. This research was explored:

- through undertaking a large-scale Australia-wide telephone survey conducted with one thousand (n = 1000) randomly selected householders stratified in proportion to the metropolitan and regional/rural distribution of the Australian population
- by conducting a focus group discussion with a representative 'slice' of the community (covering men and women, and young adults, middle-aged people and older people)

Eureka Strategic Research was commissioned to look at more complex attitudes in relation to other uses of biotechnology. The research involved a phone poll of 1067 people on broad biotechnology issues, and was supported with 13 focus groups. Participants were between 18 and 75 years of age, and selected from the White Pages, on the basis of location, gender and age to ensure that the sample was representative of the population. The survey states that a representative sample of this size provides a 95% confidence level of no more than ± 3%. That is, if 50% of the survey respondents hold a particular view, there is 95% confidence that 47–53% of the general population hold this view. This survey began in 1999 and has been repeated every two years, with the fourth wave being completed in 2005.

A number of aspects of these surveys cover areas within the Committee's terms of reference. Therefore, the results were considered by the Committee and are summarised below.[24]

Changes in attitudes over time (2002–05)

Over time, there has been a small increase in acceptance of human stem cells derived from embryos and from adults (slightly higher acceptability), with similar trends for such other technologies as genetic testing of unborn children and gene therapy for disorders and diseases. Some technologies

24. Sources used are:
Eureka Strategic Research (2005). Public Awareness Research 2005 Reports: Overview, Cloning, Stem Cells, Biotechnology Australia. All three of these reports can be found at http://www.biotechnology.gov.au/reports
An extract from Market Attitude Research Services (2005). *Key Findings Report: Human Stem Cell Research: Australian Community Public Opinion Trends and Insights* can be seen at: http://www.biotechnology.gov.au/index.cfm?event=object.showContent&objectID=51BBEA31-65BF-4956-B66FC7F1CCA2C2C5

continue to be considerably less acceptable than others — human cloning, the use of gene therapy to increase a child's intelligence or to make a child an average weight. The questions below have been asked since 2002 to explore Australian public opinion towards human stem cell issues.

Table 7.1 Percentage of respondents that selected 'approve' or 'strongly approve' in response to the question 'In relation to human stem cell issues, for each of the following situations, do you see them as being morally acceptable to society or not?'

	% of respondents that approve or strongly approve			
Year	**2002**	**2003**	**2004**	**2005**
Human stem cells being derived from embryos	53%	59%	63%	65%
Human stem cells being derived from adult cells	70%	88%	78%	78%
Human cloning	8%	6%	7%	8%
Genetic testing of unborn children	54%	61%	65%	67%
Gene therapy being used to correct genetic disorders	74%	79%	79%	78%
Gene therapy to help cure genetic diseases	77%	84%	84%	78%

Table 7.2 Percentage of respondents that selected 'approve' or 'strongly approve' in response to the question 'How strongly do you approve or not approve with changing the make-up of human cells to … '

	% of respondents that approve or strongly approve			
Year	**2002**	**2003**	**2004**	**2005**
Reduce a person's chance of getting breast cancer	70%	73%	72%	70%
Reduce a person's chance of getting heart disease	70%	72%	72%	70%
Reduce a person's chance of getting schizophrenia	70%	72%	72%	68%
Increase a child's intelligence level above normal	12%	10%	10%	13%
Make a child of average weight rather than being overweight	24%	20%	29%	27%

Public awareness research (2005)

Stem cells

Of the population surveyed, 93.4% were **aware** of medical research using stem cells, but awareness levels dropped when respondents were asked about specific types of stem cells (embryonic or non-embryonic stem cells), with a higher awareness of embryonic than non-embryonic stem cell use.

A high perceived **usefulness** of using stem cells in research (89.7%) dropped when asked specifically about embryonic (75.9%) or non-embryonic (72.4%) stem cells (Figure 7.1). This was a pattern in response to a number of questions — after generic questions about stem cell research, there was a marked shift in responses when respondents were asked the same question in relation, specifically, to embryonic or non-embryonic stem cells.

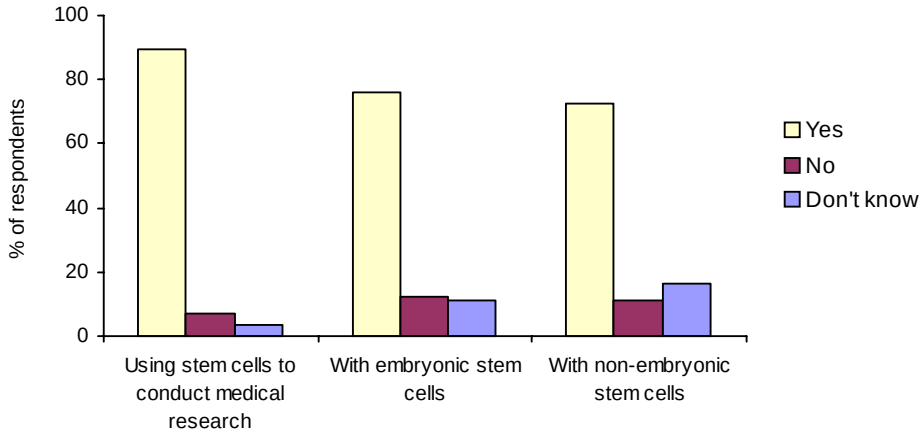


Figure 7.1 Perceived usefulness of using stem cells in research

The perceived **risks** of stem cell research overall (38.6%) were lower than for embryonic stem cell research but higher than for non-embryonic stem cell research (Figure 7.2). The **acceptability** of stem cells in research was 80% for stem cells overall, but dropped to 63.5% for embryonic, and 68.9% for non-embryonic, stem cells.

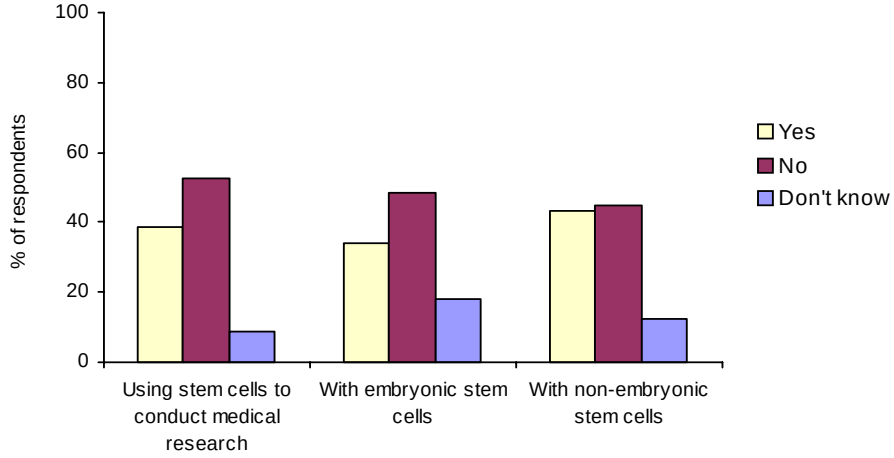


Figure 7.2 Perceived risk associated with using stem cells in medical research

A high percentage of respondents acknowledged the **usefulness** of stem cells to treat disease (87.6%), which was a higher percentage than those who saw the usefulness of gene technology to produce medicines, the usefulness of gene technology in human transplants, or the usefulness of gene technology to modify plants used for food (Figure 7.3). However, the percentage of respondents dropped once people were asked the question in relation to embryonic stem cells (to 76.4%) or non-embryonic stem cells (72.7%).

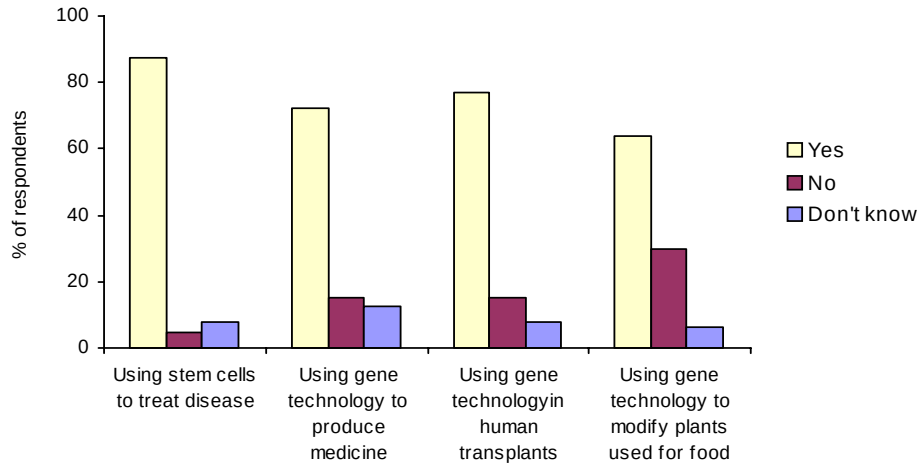


Figure 7.3 Perceived usefulness of gene technology applications

The **acceptability** of using stems cells to treat disease was 79.8%, which was again higher than when the same question was asked specifically about embryonic stem cells and non-embryonic stem cells (Figure 7.4).

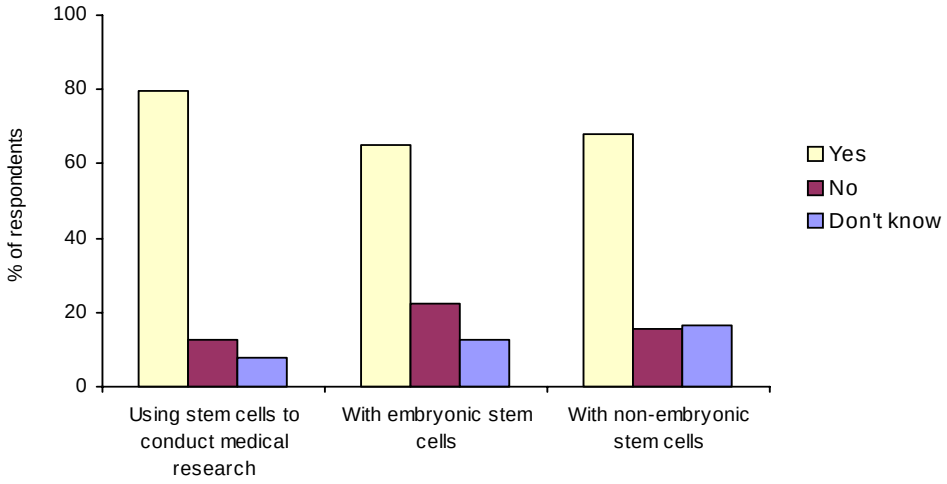


Figure 7.4 Acceptability of using stem cells to treat disease

About a third of respondents saw a risk associated with the use of stem cells to treat disease (37.0%) or to conduct medical research (38.6%).There is also a high expectation that the use of stem cells will have an effect in the short term, with 68.9% believing there is already an effect or will be in the next five years.

The qualitative research provided some insight to inform interpretation of these figures. There was considerable variation in awareness and knowledge of stem cells in the qualitative research groups, with many having heard of stem cells but having given little thought to their origin or the differences between types. There was greater familiarity with the term ‘embryonic stem cells’ than with the term (or concept) of ‘non-embryonic stem cells’.

A few participants were aware that embryos left over from IVF were often the source of embryonic stem cells, while others believed they came from a fetus. This confusion seemed to result from confusion over the terms ‘embryo’ and ‘fetus’, with some believing they were the one and the same. Others believed that umbilical cords were the source of embryonic stem cells.

The acceptability of use of embryonic stem cells appeared to depend on several factors. The origin of the stem cells was important. When informed that embryonic stem cells come from embryos, participants’ concepts of the embryo became influential, and the perception of the development or age of the embryo governed acceptability. If the embryo was considered to be a clump of cells and little more, then it was an acceptable source of stem cells; if the embryo was considered to be a baby, its use as a source of cells was less acceptable. Thus, the point at which life is understood to begin affects acceptability of embryonic stem cell use. The intention in creating the embryo was also important. Most participants did not support the creation of an embryo for the purpose of obtaining stem cells.

Cloning

The survey identified a high level (97.6%) of **awareness** of cloning in the general population, especially cloning of animals; 86.2% were aware of cloning of humans, and only 76.1% were aware of the cloning of plants, despite this being a very old technique of propagation.

Those forms of cloning that were perceived as most useful (Figure 7.5) were seen as less risky:

- 67.2% saw cloning of plants as useful, with 47.0% seeing it as risky
- 40.4% saw cloning of animals as useful, with 67.4% seeing it as risky
- 18.0% saw cloning of humans as useful, with 90.3% seeing it as risky.

Cloning of plants was seen as the most **acceptable** form of cloning (64.1%), followed by cloning of animals and cloning of humans (Figure 7.5).

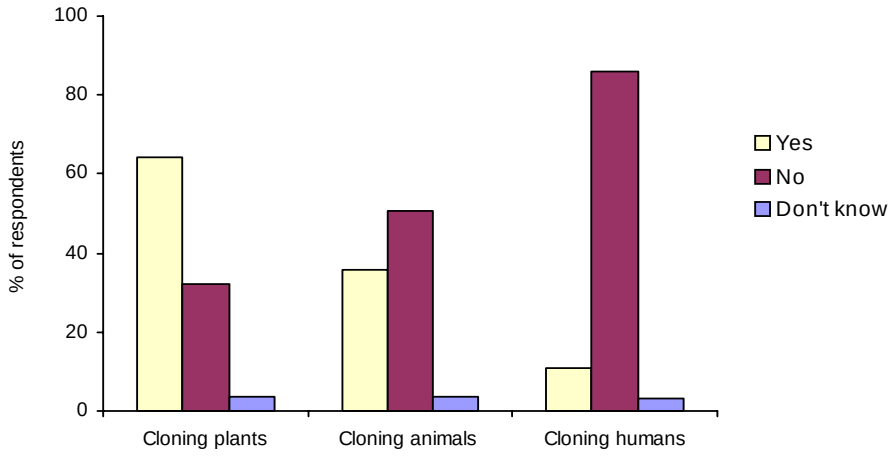


Figure 7.5 Acceptability of cloning

Qualitative focus group

Discussion in the qualitative research groups revealed various understandings of what cloning of humans might be. Human cloning was taken as the exact reproduction of an entire human, and few could understand what legitimate purpose that could have. When discussing the use of cloning to obtain body organs for transplant, most assumed this still involved cloning entire humans, and then harvesting the parts required. This would be unacceptable.

There was little understanding of many terms, such as 'therapeutic cloning' and 'nuclear transfer'. The term 'cloning' was more negatively weighted than the term 'therapeutic', which was positively weighted. That there was little understanding of these terms is an important finding, not only because it provided a deeper understanding of stem cell research, but also because it may have impacted upon the responses of the survey participants.

Overall, the Biotechnology Australia survey provides an important insight into the attitudes of the Australian public to stem cell research. However, the terms used were not defined, the survey did not seek to measure knowledge, and the focus groups suggested that many participants had limited understanding of cloning or stem cell research, all of which suggest that some caution is required when interpreting the results of this research.

7.4 Summary — community standards on the status and uses of human embryos

The Committee heard a range of arguments reflecting the diverse range of community views on the status of embryos and their creation and use in research and to develop therapeutic products.

Many submissions and discussions at the hearings focused on the moral status of the embryo and moral obligations owed to it. For some, the embryo had moral status equivalent to that of an adult person, regardless of the method of its creation or the purposes to which it could be put. For others, the moral status of the embryo varied depending upon its formation, its social relationships or its possible use (ie for research purposes or for reproduction).

Some submissions debated the relative significance of embryos formed for the purposes of reproduction and embryos formed specifically for research. For some, this distinction supported the acceptability of creating embryos (by any means) for research purposes, but prohibited their implantation in a woman. For others, the distinction was reason to sustain the current position that permits use of excess embryos, but prohibits their creation for research purposes. Similarly, for some, there was a morally significant distinction between an embryo formed by the fusion of a sperm and egg, and one formed by alternative means: the former having the social significance of being created within the context of a family; the latter being an extension of the person whose cell was used to create it (and, as such, the product of research, suitable for research purposes). Embryos formed by fertilisation may have greater significance for many people than those formed by nuclear transfer.

Proponents of embryo research emphasised the ethical imperative of pursuing the research made possible by such technologies, and argued that current arrangements already sanction the possibility of the destruction of embryos, in the context of providing ART services to infertile couples. Therefore, failing to help people with other medical problems would be unfair. Opponents, on the other hand, offered arguments based in moral views and religious traditions about the start of human life.

Use of excess ART embryos for research under a strictly regulated licensing regimen, although not supported by all respondents, appears to have been relatively well accepted as a pragmatic solution to the above dilemmas. In particular, support for donation of excess ART embryos for research is high among ART consumers. Attitudes towards creation of human embryos for research purposes, however, appeared to be much more complex and reflected, not only beliefs regarding the moral status of the

embryo, but also the cultural significance of reproduction and the social relevance of family and community relationships. For these reasons, the Committee found that, while it was difficult to logically define a moral difference between embryos formed by fertilisation and those formed by nuclear transfer or related methods, it appeared that embryos formed by fertilisation of eggs by sperm may have a different social or relational significance from embryos formed by nuclear transfer.

The findings of a 2005 survey by Biotechnology Australia on public attitudes to stem cell research and cloning showed that most people (80–90%) did not think that reproductive cloning was a useful or acceptable thing to do. However, between two-thirds and three-quarters of the people surveyed thought that embryonic stem cell research overall is useful and acceptable. The point at which life was understood to begin and the intention in creating the embryo affected the acceptability of embryonic stem cell research. However, focus group work showed that knowledge of the current clinical use of the cells and of the technologies involved is limited, which means that the results of the survey should be interpreted with caution.

8 Definition of a human embryo

8.1 Community understanding of 'embryo'

Despite its importance in developmental biology, there is no precise, scientific definition of an embryo. The earliest encyclopaedias (late 18th century) defined an embryo as the first rudiments of an animal in the womb, before the 'members' are distinctly formed (after which it was defined as a fetus).

In the 19th and early 20th centuries, textbooks of embryology focused on the appearance and development of organs and external features; little was known of the earlier stages, which were often referred to as an 'ovum' ('segmentation stages of the human ovum', '14-day ovum', and so on). Thereafter, more precise scientific language was developed for the stages leading to organ development, and the term 'embryo' was largely relegated to nonscientific usage. This approach is still common in medical texts. For example, *Black's Medical Dictionary*, 38th edition (Macpherson 1995) defines an embryo as 'the fetus in the womb prior to the second month'. Furthermore, the definition of 'fetus' in the same dictionary includes the following:

> The ovum produces not only the fetus but several other membranes and appendages which serve it until birth and are then cast away … The remainder of the ovum, which within two weeks of conception has increased to about 2 mm (1/12 inch) in size, splits into an outer and inner shell … From two weeks after conception onward … the name of embryo being applied to the developing being while almost indistinguishable in appearance from the embryo of other animals until the middle of the second month when it begins to show a distinctly human form.

By contrast, the current *Encyclopaedia Britannica* defines an embryo as:

> ... the early developmental stage of an animal while it is in the egg or within the uterus of the mother. In humans the term is applied to the unborn child until the end of the seventh week following conception; from the eight week the unborn child is called a fetus.[25]

Developments in ART over the past three decades have made it more important to provide an adequate biological and legal definition of an embryo. Before developments in stem cell research and human cloning made possible the creation of an embryo through somatic cell nuclear transfer (SCNT) and related techniques, legal definitions of a human embryo were only concerned with an embryo created by fusion of an egg and a sperm.

As noted in Section 2.5, before the national legislation was passed in 2002, three States (Victoria, Western Australia and South Australia) had legislation covering research on human embryos. In Victoria, the *Infertility Treatment Act 1995* (Vic) defined a human embryo as:

> … any stage of embryonic development at and from syngamy.

'Syngamy' was defined as:

> ... that stage of development of a fertilised oocyte [ovum] where the chromosomes derived from the male and female pronuclei align on the mitotic spindle.

The stages of human development from the commencement of penetration of an oocyte by a sperm up to but not including syngamy were defined as a zygote.

25. See http://corporate.britannica.com/library/online/bol.html

In Western Australia, the *Human Reproductive Technology Act 1991* (WA), defined a human embryo as:

> … a live human embryo, in the stage of development which occurs from the completion of the fertilisation of the egg or the initiation of parthenogenesis to the time when, excluding any period of storage, 7 completed weeks of the development have occurred.

Before that stage, the egg was referred to as an 'egg in the process of fertilisation'.

In South Australia, the *Reproductive Technology Act 1988* (SA), and associated Reproductive Technology (Code of Ethical Clinical Practice) Regulations 1995, did not define the term embryo.

Similarly, in the United Kingdom, s1(1) of the Human Fertilisation and Embryology Act 1990 defines embryo as follows:

> (a) an embryo means a live human embryo where fertilisation is compete, and
>
> (b) references to an embryo include an egg in the process of fertilisation,
>
> and, for this purpose, fertilisation is not complete until the appearance of a two cell zygote.[26]

In response to discussion about the definition of 'human embryo' in the current legislation, a discussion paper entitled *Human Embryo — A Biological Definition* (NHMRC 2005) was considered by the Committee during the reviews (see Section 3.3).

This chapter briefly summarises the Licensing Committee discussion paper and the other submissions and hearings with respect to the biological definition of a human embryo and human embryo clone.

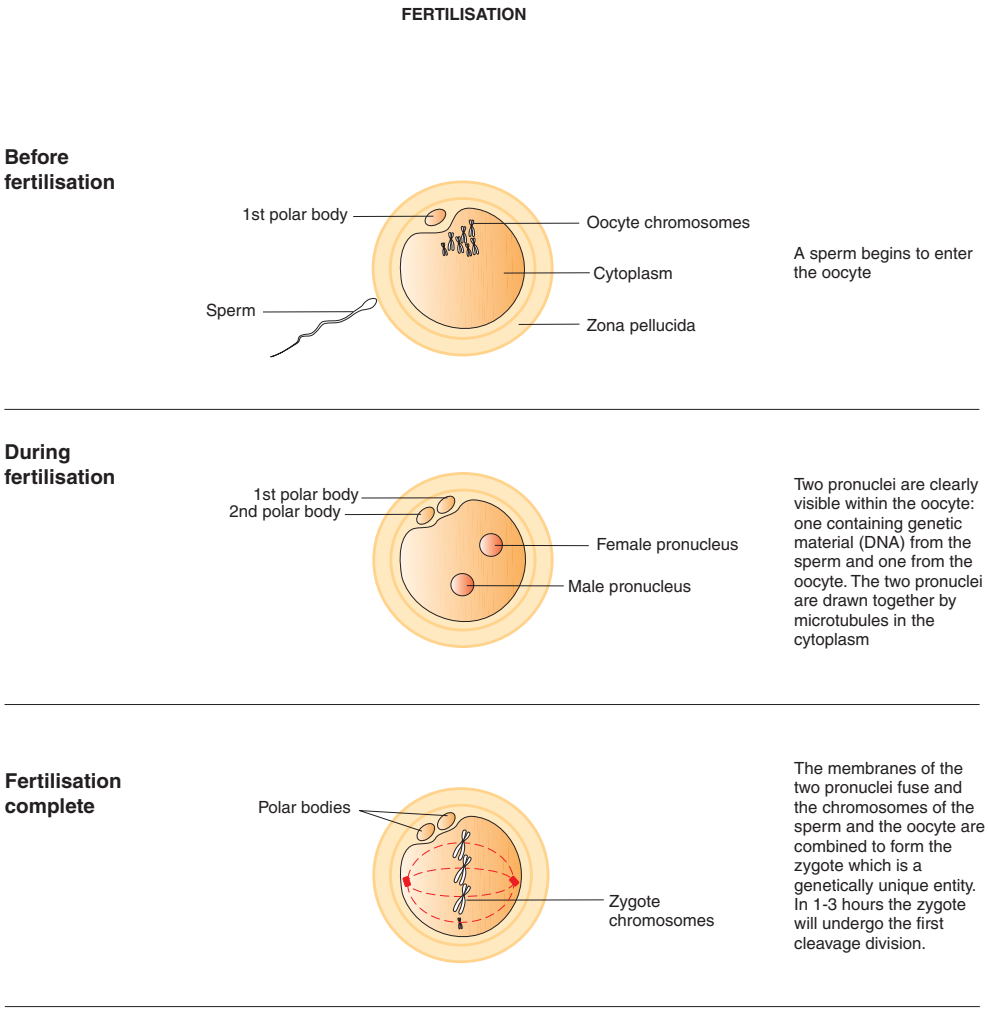
8.2 Licensing Committee report on the biological definition of a human embryo

The Licensing Committee discussion paper identifies the two main schools of thought about the biological definition of embryo:

- broad definition — that a conceptus is an embryo from the moment of its creation
- restricted definition — that a conceptus should be referred to as an embryo only after gastrulation, at which time the cells that will give rise to the future human being can be distinguished from those that form extraembryonic tissues (placenta, cord, membranes, etc).

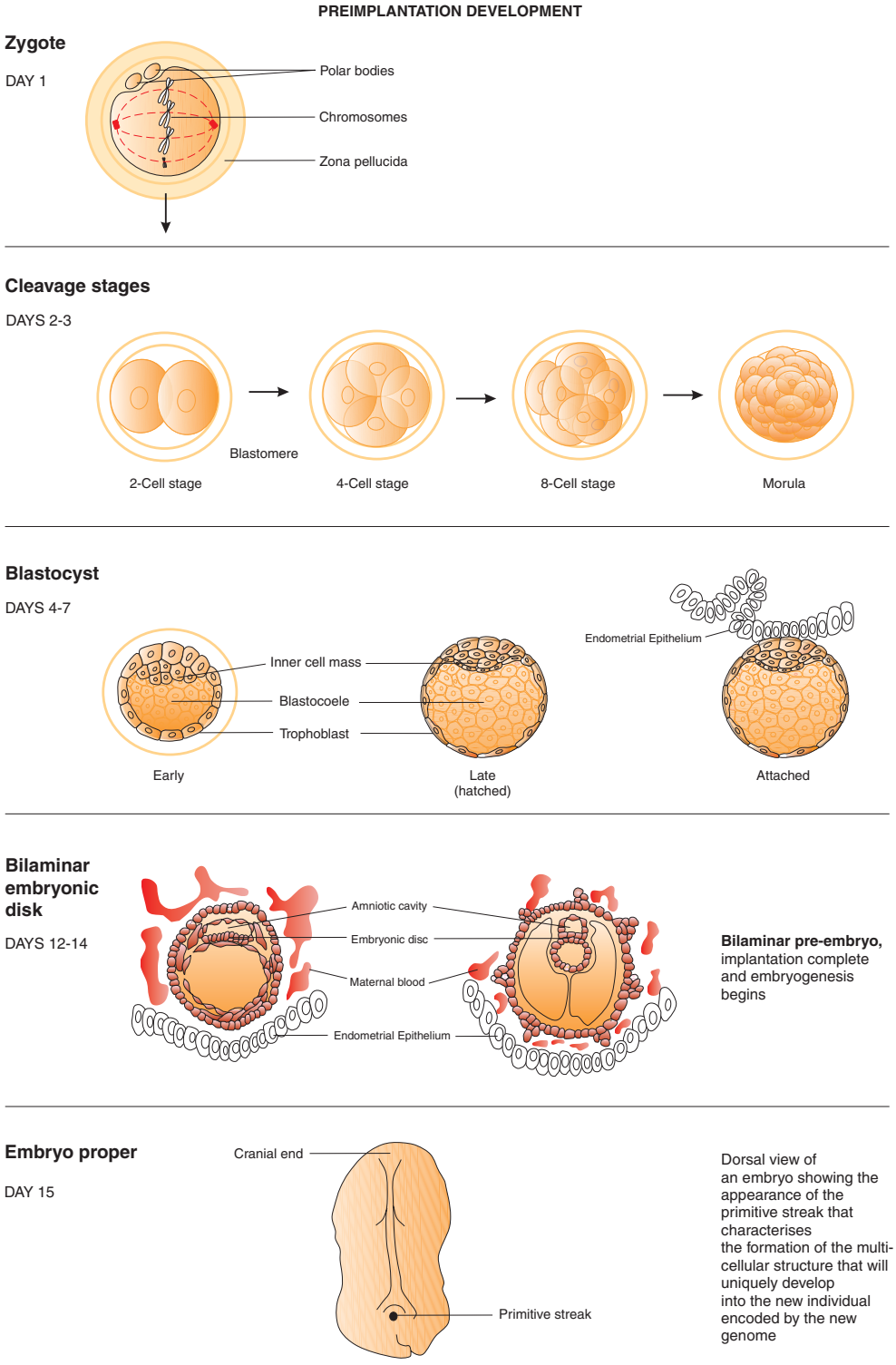
Figures 8.1 and 8.2 show the stages of fertilisation and early embryonic development to implantation and appearance of the 'primitive streak'. The appearance of the primitive streak, at about 15 days, is the first developmental point at which a multicellular structure is formed that will develop into the new individual encoded by the new genome.

26. See http://www.opsi.gov.uk/acts/acts1990/Ukpga_19900037_en_2.htm#mdiv1



Source: *Discussion Paper: Human Embryo — A Biological Definition* (NHMRC 2005)
(Sue Panckridge, graphic artist, Prince Henry's Institute of Medical Research)

Figure 8.1 Stages of fertilisation



Source: *Discussion Paper: Human Embryo — A Biological Definition* (NHMRC 2005)
(Sue Panckridge, graphic artist, Prince Henry's Institute of Medical Research)

Figure 8.2 Stages of early embryonic development up to implantation and development of the primitive streak

The discussion paper describes a number of naturally occurring variations in this process in order to develop some principles for defining an embryo. In particular, the paper considers whether these entities show:

- an integrated organisation
- the capacity for self-directed active development
- a defined genetic identity (established from the beginning of development).

For example, identical (monozygotic) twins develop by splitting of the single conceptus and therefore have the same genome. Nevertheless, each is independently considered to be a human embryo, indicating that having a unique genome cannot be considered a requirement for the biological definition of an embryo.

Similarly, chimeras can form naturally when two different embryos fuse (either in vivo or in vitro), and the resulting entity can develop to birth and is therefore considered to be an embryo. Finally, a range of chromosomal errors can lead to embryonic entities that have some capacity for development but not to the point of a live birth — for example, conditions such as ‘blighted ovum’ (an embryonic pregnancy) or various classes of trophoblastic disease (arising from abnormal fertilisation events), where the entity formed has no potential to develop into a fetus. These entities are not generally considered to be embryos.

The Licensing Committee discussion paper also describes nuclear transfer and other emerging technologies for creating embryo clones or similar bioengineered entities, in terms of the potential for development of such entities to each of the stages shown in Figures 8.1 and 8.2. For SCNT, embryo splitting, chimeric embryo formation, pronuclear transfer involving maternal and paternal pronuclei, and fertilisation of oocytes using gametes derived from embryonic stem cells, animal studies have shown that such entities can result in a live birth (although it is not known if this would be the case for humans). However, parthenogenetic development of oocytes has not been shown to progress past the early implantation stage in animals. In animal studies, pronuclear transfer involving either two male or two female pronuclei can give rise to a fetus, but not to a live birth.

The Biological Definition of a Human Embryo Working Party concluded that the significance of completion of fertilisation of a human oocyte by a human sperm was sufficient to define an entity as a human embryo, regardless of any potential (or lack of potential) for future development. It also concluded that the most appropriate marker for the completion of fertilisation is syngamy, because this is when the genome of the new entity is created. However, as syngamy is itself difficult to visualise, the earliest defined point after it has occurred is the first cell division (cleavage).

Because a number of emerging technologies produce entities that do not involve the contribution of DNA from both sperm and egg or the completion of a syngamy step (eg SCNT, parthenogenesis), the requirement for fertilisation and/or syngamy is not sufficient for the biological definition of a human embryo. In these cases, the working party suggested that whether or not an entity produced by an emerging technology should be called an embryo could be based on the potential for continued development towards a new living being. In this respect, the most appropriate marker for defining the potential for continuing development may be the appearance of the ‘primitive streak’ because it is at this stage that the multicellular entity that will form the new individual first appears.

Finally, the working party suggested that, because some techniques have the potential to produce a new individual with DNA from more than one species (hybrids or chimeras), the biological definition of a human embryo should not specifically exclude an entity created with DNA from two species.

Combining these considerations, the working party suggested the following definition:

> A human embryo is a discrete entity that has arisen from either:
>
> (a) the first mitotic division when fertilisation of a human oocyte by a human sperm is complete; or
>
> (b) any other process that initiates organised development of a biological entity with a human nuclear genome or altered human nuclear genome that has the potential to develop up to, or beyond, the stage at which the primitive streak appears,
>
> and has not yet reached eight weeks of development.

Definition of 'live' and 'viable' embryos

The current definition of human embryo in both the Acts also refers to a 'live embryo' ('a human embryo is defined as a live embryo…'; see Section 2.1). The Licensing Committee has issued the following guidance to assist potential applicants to decide whether they need to apply for a licence:[27]

> An embryo is considered to be a live embryo unless:
>
> – When maintained in suitable culture conditions, the embryo has not undergone cell division between successive observations not less than 24 hours apart, or
>
> – The embryo has been allowed to succumb by standing at room temperature for a period of not less than 24 hours.

The PHC Act also uses the term 'viable' human embryo:

> A person commits an offence if the person removes a human embryo from the body of a woman, intending to collect a viable human embryo. [PHC Act, s19]

The Committee interpreted 'viable' to mean a live embryo.

8.3 Submissions and hearings

Biological definition of a human embryo

The definition of 'human embryo' in the legislation is a very broad definition, reflecting the common understanding of 'embryo' as the developing organism from fertilisation until about eight weeks of development (after which it is a fetus). Some argued that the term 'embryo' should not be used for the entire product of the fertilised egg, much of which differentiates into tissues that will not form part of the developing person. For example, a submission from 75 third-year Bachelor of Biomedical Science students, University of Melbourne, argued that only at gastrulation does the group of cells that will develop into the future person become clearly differentiated from the other cells (as the 'primitive streak'):

> We believe that the current definition of 'human embryo' and its legal treatment in the Act fail to draw a reasonable distinction between the early and late embryo. It is debatable whether the human conceptus in the first 14 days of its development should be considered an embryo at all … The UK does not grant the embryo any legal protection until the formation of the primitive streak, 14 days into development. Even if the Australian Government is unwilling to follow the example of the UK, there is a strong case for allowing experimental manipulation of the early conceptus, given that knowledge gained from research involving embryos may be used to ease the suffering of living and conscious humans with currently incurable diseases. *Third-year Bachelor of Biomedical Science students, University of Melbourne (Submission LRC449)*

27. How to decide when an excess ART embryo is alive or dead. In: *Procedural Guidance for Applying for a Licence*, NHMRC, August 2003. http://www.nhmrc.gov.au/embryos/monitor/application/guide.htm#1

Although the term ‘zygote’ is defined as the one-cell stage of embryonic development, it is difficult to clearly identify and define this stage. Approximately 20 hours after the sperm enters the oocyte, the pronuclear membranes dissolve and the maternal and paternal chromosomes combine. Almost immediately (and without reformation of a nuclear membrane), the chromosomes align for the first cell division (a process known as syngamy). Strictly speaking, the zygote stage covers the time from syngamy to first cell division. However, the absence of nuclear membranes at this stage means that the only way that it can be confirmed that syngamy has occurred is when the cell divides (NHMRC 2005). Thus the zygote stage of human embryonic development is visually elusive and hence there has been a tendency to refer to visible milestones, such as formation of the pronuclei (as for the current definition in the RIHE Act) or the first cell division.

In an attempt to distinguish the single cell stages before and after the combination of maternal and paternal chromosomes, some scientists have used the term ‘pre-embryo’ for the former. Other scientists have also used this term to distinguish all the stages of development up to implantation (ie to distinguish between the broad and restricted definitions of embryo). However, other scientists and bioethicists have cautioned against this approach:

> … there was an astounding avoidance of defining the term ‘human embryo’ … This was due to the control of the various institutional committees by the scientists who coined the term ‘pre-embryo’ to obfuscate their research and to bewilder their critics and the general public on the ‘ethical status of the human embryo’. *Dr Joseph Santamaria, President, Family Council of Victoria (Submission LRC381)*

> A human embryo is one that is created by either the fertilization of human egg by human sperm or by some other means of initiating life such as human cloning. The means used in its creation is irrelevant to its status. To alter the terminology when describing a human embryo, so as to blur the truth of its origins and status, is deceitful and should be avoided.
> *Australian Family Association (New South Wales) (Supplementary submission LRC259)*

> The inclusion of all viable embryos, regardless of the means of production, should be retained. We oppose any attempts to introduce confusing and irrelevant designators such as ‘pre-embryo’ into the legislation. *Anglican Church of Australia, Sydney Diocese (Submission LRC780)*

Professor Louis Waller, Monash Law, Monash University, added that the language used to frame any legislation or regulations should be carefully chosen, and that people who draft the definition of ‘embryo’ should be aware of its ambit:

> … the insertion into a human oocyte which has been denucleated of a somatic cell taken from a person with view to then developing what is conveniently, but I think perhaps in some ways improperly, called an embryo, is in effect an issue about language … in some of the debates that have taken place as a consequence in the field of infertility treatment, an expression pre-embryo has been cordoned, particularly in the United States, and it’s achieved a measure of acceptance amongst both medical practitioners, people interested in ethics and lawyers…
> *Professor Louis Waller, Monash Law, Monash University (Melbourne hearings)*

An argument that was raised by a number of respondents for not using the restricted definition of an embryo was that, although the cells of the early stages are not all destined to become part of the developing person, the whole developmental process is directed by the genetic entity formed at fertilisation.

> Recent research indicates that a human embryo puts up a defensive mechanism to fight off the attacks of the mother’s immune system. In a landmark paper released in 1998 by researchers at the Medical College of Georgia in Augusta USA discovered that the ‘IDO’ [indoleamine 2,3-dioxygenase] (which suppresses the mother’s T cell reaction) allows pregnancy to continue … This research shows that the embryo begins its defence at day 6 just prior to attaching to the uterus wall and drawing on the mother’s food supplies. The point that is important to think about is that the embryo is a separate, individual entity that right from the beginning is more than a blob of cells. Thus the termination of an embryo is the death of a human. *Mr Rick Maude, New South Wales (Submission LRC316)*

The Caroline Chisholm Centre for Health Ethics Inc thought that the distinction between totipotency and pluripotency (see Section 5.1) is useful to underpin the definition of a human embryo:

> … a legal definition of the human embryo is needed which can be applied to all genuine human embryos, but not to apparent human embryos. The notions of potency, totipotency and actuality need to be employed in the definition of an embryo … Pluripotent cells need to be clearly distinguished from totipotent cells. Caution would suggest leaving the law as it is until the dispute is resolved beyond reasonable doubt. *Caroline Chisholm Centre for Health Ethics Inc (Submission LRC392)*

> From a philosophical viewpoint, a human embryo may be defined as a totipotent cell or a group of cells or a multicellular organism, which due to its genome, has the inherent actual potential to continue organised human development in a suitable environment. *Caroline Chisholm Centre for Health Ethics Inc (Submission LRC392)*

This definition does not distinguish a human embryo clone from a human embryo created by fertilisation, as both are totipotent. However, it can be used to distinguish embryonic stem cells and any activated cell derivatives of them that do not have the potential to develop into a whole organism.

Some submissions highlighted the circular nature of the current definition:

> It [the Act] defines an embryo by using the term embryo so that it doesn't distinguish a human cell that is capable of some development from a human cell that is oriented to that particular type of development that may result in a child being born given a favourable environment … *Associate Professor Bernadette Tobin, Director, Plunkett Centre for Ethics, Australian Catholic University (Sydney hearings)*

> The definition of human embryo … is well intended, but inadequate because circular. This inadequacy may in fact mean that these Acts do not prohibit and/or regulate what they are supposed to prohibit and/or regulate. *Father Gerald Gleeson, Catholic Institute of Sydney (Submission LRC379)*

> … this definition of a human embryo gives no clarity as to what a human embryo essentially is, or what conditions are required before it is concluded that an embryo now exists. There is nothing in the definition that distinguishes a human cell that is capable of some type of development … and those which are oriented toward resulting in a child being born. The definition is of no assistance in discriminating between 'hybrid embryos', 'chimeric embryos', and cloned embryos or embryos formed using animal cells. *Queensland Right to Life (Submission LRC376)*

Many other respondents, however, stated that they had not found the current definition to be ambiguous (with the exception of the issues of oocyte activation and parthenogenesis; see below). However, many concerns were raised about the broader scientific and community understanding of 'embryo', and the Committee heard a number of different views about the complex scientific, social and ethical issues relating to the use of this term, which are discussed below.

Overall, respondents stressed the need for the definition of an embryo to be completely honest and 'forthright' so that any prohibition and permissions (such as those covering the creation of certain types of embryos for research) are completely transparent within this framework. At the Melbourne hearings, Reverend Dr Colin Honey, Chair, Stem Cell Ethics Australia, warned about changing terminology:

> I'm suspicious of the motives of those that want to change the terminology … The purpose is to prevent the public from becoming concerned about this particular area, which is most certainly cloning and early cloning, though it be for a therapeutic purpose. And it would seem to me terribly important that the public not come to the view that they are having the wool pulled over their eyes and I think it's in the best interest of the science that that be the case.
> *Reverend Dr Colin Honey, Chair, Stem Cell Ethics Australia (Melbourne hearings)*

Similarly, both Associate Professor Bernadette Tobin, Director, Plunkett Centre for Ethics, and Professor Louis Waller, Monash University, stressed the importance of using clear and unambiguous language. At the Melbourne hearings, Professor Waller said:

> … language should therefore be employed which makes it clear that this is what this legislation is about and this is what it is designed to regulate … What must be avoided is … any sleight of hand — any linguistic sleight of hand. The cards must be clearly turned up on the table so that the whole community is made as aware as possible of what new legislation is designed to do and what it's designed to prohibit, what it's designed to permit albeit it with very, very careful regulatory processes. *Professor Louis Waller, Monash Law, Monash University (Melbourne hearings)*

Biological definition of a human embryo clone

Several respondents commended the definition of a human embryo clone in the PHC Act for clearly stating that a human embryo clone is a human embryo:

> The Lockhart definitions used in the 2002 legislation's explanatory notes, must be commended for their honesty in stating that cloned human embryos are quite able to develop to birth. *Mr Basil Bryan, Tasmania (Submission LRC295)*

> I commend the existing Lockhart definitions in recognizing that cloned embryos are human embryos like any other, are alive and have the potential of being carried to birth. *Mr Luke Scott, New South Wales (Submission LRC299)*

On the other hand, others said that it was not clear why a human embryo clone needed to be defined as an embryo. At the Adelaide hearing, Associate Professor Wendy Rogers, Department of Medical Education, Flinders University, told the Committee that it was not clear that an SCNT clone should be called an 'embryo'. If it were not defined as an embryo, there would not be a problem with creating one.

Still others warned that the term 'human embryo clone' is ambiguous in terms of the intended use of the embryo clone:

> The current terminology may lead to the mistaken belief that the intended use of the 'human embryo clone' is only to create a 'cloned' human. This ignores the potential use of this technology to generate stem cells for research, a use that many consider reasonable and potentially extremely beneficial. The term 'human nuclear transfer embryo' is more appropriate as it clearly and unambiguously states the method of derivation. *Stem Cell Sciences Ltd (Submission LRC318)*

Finally, as with the definition of human embryo, respondents stressed that the definition of a human embryo clone needs to be honest and rigorous but at the same time flexible enough to cover all the emerging technologies in this area:

> It is desirable that the definition in the legislation be broad enough to cover all the possible mechanisms of 'artificially' creating a human clone (both presently available and those conceivable in the future). Such a definition should not depend on the intended use of the cloned embryo, but remain a purely biological description. *Anglican Church of Australia, Sydney Diocese (Submission LRC780)*

Some respondents referred to the definition of nuclear transfer and related technologies rather than the definition of the embryo so formed. Stem Cell Sciences Ltd (Submission LRC318) indicated that 'somatic cell nuclear transfer' should be defined in the legislation. Others stressed that the legislation needs to keep pace with changes in the technology to ensure that it is not possible to create an embryo using new techniques for the purposes of reproduction:

> … one of the problems that you are going to face if somatic cell nuclear transfer became legalised is drawing up legislation in a very rapidly changing field. Terms like somatic cell nuclear transfer are likely to be joined by a lot of other new terms describing new modifications of this technology that are coming on line now. For example, 'altered nuclear transfer' is the term for a proposed method to genetically modify a somatic cell so that you derive a blastocyst that can not implant. It has not been shown whether this is scientifically feasible or not … but you have to forecast it at least terminologically in the definitions … Otherwise you'll find that the legislation will be falling over its feet almost as soon as it's written. *Associate Professor Melissa Little, Institute for Molecular Bioscience, University of Queensland (Brisbane hearings)*

8.4 Summary — definition of a human embryo

The general community understanding of 'embryo' is very broad (including the whole time from conception to the time when it becomes a fetus at eight weeks after conception). However, the medical and scientific community has used a more restricted definition of embryo — referring only to the developing entity after gastrulation, at which time the cells that will give rise to the future human being (the 'embryo proper') can be distinguished from those that form extraembryonic tissues (placenta, cord, membranes, etc).

The Australian legislation and most other legislation to date have defined an embryo according to the broad community understanding. However, the RIHE Act and PHC Act place more precise boundaries on the definition than would normally be the case. While there has been no disagreement about the later boundary (eight weeks after conception), the earlier boundary is harder to pinpoint, especially for embryos created by means other than by fertilisation of an egg with sperm.

The NHMRC has reviewed the stages of embryonic development after fertilisation, natural anomalies that can occur in this process, and the different ways that it currently appears possible to create an entity that may be defined as a human embryo (NHMRC 2005). As a result, the working party recommended a definition that distinguishes two ways of creating human embryos:

- those formed by fertilisation of a human oocyte by a human sperm (in which case the entity should be defined as a human embryo from when the first cell division is complete)
- those formed by any other process and that have the potential to develop up to, or beyond, the stage at which the primitive streak appears.

In the first case, inclusion in the definition of human embryo stands regardless of any potential (or lack of potential) for future development. It is enough that the embryo was formed by fertilisation. The first cell division is given as the marker for the start of this phase as it is the first visible sign that a new genetic entity has been formed (after combining of the nuclear material from the egg and the sperm at syngamy). However, in the second case, in which initiation of development is by some other means, the working party suggested that the potential for continued development towards a new living being is the most important attribute for defining such an entity as a human embryo.

These definitions accord with the positions of most of the respondents in the reviews, as they preserve the special position of fertilisation in the formation of a human embryo and uphold the broad community understanding of an embryo as something that is able to continue development in an integrated way to become a fetus and live baby. This definition also provides a flexible framework for consideration of new technologies.

9 Licensing arrangements

9.1 Overview of Licensing Committee activities

Under the RIHE Act, research involving excess assisted reproductive technology (ART) embryos can only be done under licence granted by the Embryo Research Licensing Committee of the NHMRC (the Licensing Committee). The Act establishes the Licensing Committee as a principal committee of the NHMRC with nine members appointed by the Australian minister with portfolio responsibility for human cloning and embryo research, in consultation with the States and Territories (see Section 2.2). The functions of the committee are to:

- consider applications for licences to use excess ART embryos
- refuse or grant licences, subject to conditions
- maintain a publicly available database containing information about licences issued
- monitor activities and ensure compliance with the legislation through appointment of inspectors, and take necessary enforcement action, such as cancelling or suspending licences
- report to the Australian Parliament at six-monthly intervals on the operation of the RIHE Act and the licences issued under the Act.

The Licensing Committee was appointed in March 2003 and since that time has developed policies and procedures, issued several guidance documents, assessed applications for licences and applications to vary licences, established a public database, received reports from the inspectors appointed under the RIHE Act, and prepared and tabled reports to parliament. In developing policy, the Licensing Committee has worked closely with another principal committee of the NHMRC, the Australian Health Ethics Committee (AHEC). The Licensing Committee meets regularly in person and by teleconference.

The Licensing Committee has issued nine licences to date, which authorise the use of a total of 1735 embryos (see Chapters 4 and 5). Of these, four permit the use of embryos to derive embryonic stem cell lines, four are for improvements in ART, and one allows training of embryologists in embryo biopsy techniques. The licences contain conditions specifying the number of embryos that may be used, any restrictions on the use of the embryos, and recording and reporting requirements, among other things. A substantial component of the Licensing Committee's work during the past year has been the consideration of applications to vary existing licences, including both administrative changes to the licence and changes to the approved project.

Another important function of the Licensing Committee has been to develop a program of activities for communication with stakeholders. These activities include presentations by members of the Licensing Committee at various meetings, visits to applicants by committee members and secretariat, production of information bulletins about the committee's activities, and a training workshop for human research ethics committee (HREC) members.

Cost recovery

The costs of supporting the Licensing Committee and the national compliance system are significant. The Australian Government Portfolio Budget Statement for the financial year 2003–04 indicates a total commitment of $3.3 million per year. To date, no cost recovery mechanism has been applied to recover these costs.

The Productivity Commission recently undertook a review of cost recovery in government agencies: *Cost Recovery by Government Agencies* (Productivity Commission 2002).[28] Recommendation 7.9 of that report states:

> As a general principle, the administrative costs of regulation should be recovered, so that the price of each regulated product incorporates the cost of efficient regulation. Cost recovery should not be implemented where:
>
> – it is not cost effective;
>
> – it would be inconsistent with policy objectives; or
>
> – it would unduly stifle competition and industry innovation.

The Productivity Commission also stated that the purpose of cost recovery is to improve the efficiency with which the government uses its resources. The Commission recommended that cost recovery arrangements that are not justified on grounds of economic efficiency should not be undertaken solely to raise revenue for government activities.

Considering the small number of licence applications received, it is unlikely that introducing cost recovery would be cost-effective or efficient. In addition, organisations are already meeting the costs of compliance with the national regulatory scheme and, in relation to compliance with licensing requirements, these costs may be significant.

The national system applies across all organisations undertaking relevant activities, irrespective of whether or not they apply for or receive a licence. Therefore, targeting licence applicants and licence holders for cost recovery may place an unfair burden on these organisations. Indeed, if total costs were to be recovered from licence holders only, this cost would be exorbitant and would apply a strong disincentive to application, thus inhibiting the research that the system was established to enable.

9.2 Submissions and hearings

The Committee received a number of submissions referring to strengths and weaknesses of the licensing system, including a detailed submission from the NHMRC (Submission LRC790). In addition, the Committee met with the Licensing Committee in Adelaide to discuss the issues that were subsequently raised in the NHMRC written submission. The remainder of this chapter summarises the information received by the Committee in the written submissions and hearings, and the meeting with the Licensing Committee.

NHMRC submission and meeting with Licensing Committee

General observations about the licensing system

The NHMRC submission (Submission LRC790), which included detailed comments from the Licensing Committee, identified a number of challenges that the Licensing Committee has had to confront. The Licensing Committee recognised that the time taken for issuing the first licences was lengthy, but explained that this was an unavoidable aspect of establishing a new regulatory system:

> The LC issued the first licences 12 months after the Committee was appointed, that is 18 months after the legislation was passed. However, during that time, the LC has been required to concurrently receive applications for licences, develop policy and procedures to underpin the legislation, develop its relationship within the NHMRC structures and engage a community with a heightened expectation of what the implications of regulating embryo research would be. *NHMRC (Submission LRC790)*

28. See http://www.pc.gov.au/inquiry/costrecovery/finalreport/index.html

> When the LC was considering early licence applications and simultaneously developing policy and procedures, its activities were slowed by misunderstandings about the information required in applications. The LC engaged in extensive consultation and repeated rounds of question and answer in order to obtain the information it required to make a decision. Members of the LC and Secretariat also visited applicants to discuss the applications more efficiently. These activities all contributed to the perception that the LC was slow to make decisions. However, it also demonstrated the LC's willingness to communicate with applicants to help them improve their applications and its determination to observe all the requirements of the RIHEA. *NHMRC (Submission LRC790)*

In reaching decisions about licence applications, the Licensing Committee has to strike a balance between two requirements in the RIHE Act; that is, the need to restrict the number of excess ART embryos to that likely to be necessary to achieve the goals of the research project, and the need to take into account the likelihood of significant advance in knowledge or improvement in technologies for treatment as the result of use of the excess ART embryos. There is a tension between these two elements:

> The licence must permit the use of sufficient embryos to give a reasonable chance of achieving the goals of the project. There is little value in permitting an experiment to be conducted but preventing the use of the necessary number to give statistical validity to the results. *NHMRC (Submission LRC790)*

With regard to the use of excess ART embryos for training or quality assurance activities, the Licensing Committee has found that determining whether these activities could be considered to have the potential to provide a 'significant advance' has been less straightforward than for research activities:

> It is apparent from the Explanatory Memorandum that Parliament considered training to be an acceptable use of excess ART embryos provided all the requirements of the RIHEA could be satisfied. Consequently, the Committee has issued a licence for training embryologists and expects that there may be a need for additional training licences in the future. *NHMRC (Submission LRC790)*

> The situation is less clear with respect to the use of excess ART embryos for quality assurance activities. Although quality assurance is included in the Explanatory Memorandum as an activity which is permitted by the RIHEA, the LC has not fully resolved its views on it. The LC has not yet needed to make a decision but will do so if it considers applications for quality assurance activities. *NHMRC (Submission LRC790)*

The scope of the RIHE Act has presented the Licensing Committee with another challenge:

> The scope of the RIHEA is limited to the use of excess ART embryos which is challenging for two reasons. The first is the public perception that the legislation regulates research involving stem cells when it doesn't, and the second is that when embryos are used for deriving embryonic stem cells, the regulation does not extend to the use of those embryonic stem cells lines. *NHMRC (Submission LRC790)*

Another observation made in the NHMRC submission was that communication with consumer stakeholders has not always been successful:

> The LC has sought to engage with a broad community of interests including the general public. This has been undertaken in a systematic manner with the identification of the research community as a priority. However, some target audiences have been difficult to reach, including consumers. *NHMRC (Submission LRC790)*

The Licensing Committee has not received any new licence applications since October 2003. In the NHMRC submission (Submission LRC790), the Licensing Committee suggested that this could be due to the perception that the committee is slow to make decisions, the possibility that some researchers are waiting for the reviews of the legislation to be completed, or lack of availability of excess ART embryos.

Interpretation and operation of the RIHE ACT

As indicated above, the Licensing Committee has spent much time considering the requirement in the RIHE Act for the committee to take into account the likelihood of 'significant advance' as a result of the training and quality assurance activities proposed in the licence.

There has been some difficulty in interpreting the meaning of the Act with regard to exempt uses of excess ART embryos. Licence holders have queried whether thawing of an embryo should be considered as part of the licensed activity; this is important because it may mean that only those people authorised by the licence are permitted to thaw embryos before their use in a licensed activity. The Licensing Committee has suggested that s10 of the RIHE Act requires amendment to remove this ambiguity (Submission LRC790).

The NHMRC submission noted that the RIHE Act does not specify the status of embryos that are unused after a licensed activity. The Licensing Committee has developed a standard condition to cover this situation, but queried whether this condition should be dealt with in the Act rather than the licence:

> If the embryos are not used the consent becomes ineffective and the embryos cannot be used for another project without going back to the responsible persons to request consent for that new project. Thus the condition requires that the licence holder must transfer unused embryos back to the ART clinic they came from, or, if the licence holder is also the ART clinic, approach the responsible persons for new consent … The LC recommends that the LRC consider whether the status of excess ART embryos unused at the end of a licence or project needs to be covered by the RIHEA rather than by administrative processes such as a condition of licence. *NHMRC (Submission LRC790)*

The Licensing Committee expressed frustration that its regulatory role is restricted to oversight of the use of the embryo, with no ability to oversee the steps that occur after the embryo has been destroyed by removal of the inner cell mass. This makes it difficult for the Licensing Committee to evaluate whether a licence has achieved its stated goals. This restricts the ability of the Committee to take into account the likelihood of significant advance arising from the licence application:

> It is important for the LC to be able to evaluate the effectiveness of the licences issued particularly with respect to the likelihood of significant advance and the minimum number of embryos. It is difficult for the LC to gather this information when its regulatory role is limited, particularly when control of the outcome passes from the licence holder to a third party. For example, the LC would like to know how many stem cell lines result from the number of embryos authorised for use in each of the stem cell licences … In an attempt to gain more information about the success and effectiveness of the licences, the LC recommends that it have the power to require a mandatory report from the licence holder within 12 months of the licence's expiry because this would help them obtain more information about the achievements of each licensed use of excess ART embryos. *NHMRC (Submission LRC790)*

A similar issue arises when applications are submitted by two collaborating organisations. A licence can only be issued to a single organisation — the organisation on whose premises the embryo will be damaged or destroyed — and subsequent work on the cells isolated from the embryos at the collaborating organisation is outside the Licensing Committee's oversight. The Licensing Committee identified this as a problem both with respect to assessing the potential for 'significant advance' and also for monitoring and compliance, and suggested that the difficulty would be overcome if there were a capacity in the Act for licences to be held jointly by two organisations:

> Because regulatory control relates to the use of the embryo (and not to steps that occur after the embryo has been used), the LC has had to put in place sometimes complex administrative arrangements to ensure appropriate oversight of work being undertaken across different organisations. This has been most evident with some of the licences involving the development of embryonic stem cell lines, where the use of the embryo and initial isolation of stem cells occurs in one organisation and development of the cell lines occurs in a second organisation. One avenue to address this is to provide for the capacity to have joint licence applicants and holders, to confer the obligations for the provision of information and reporting on all organisations involved. *NHMRC (Submission LRC790)*

Another shortcoming identified in the RIHE Act by the Licensing Committee was the lack of powers surrounding suspension or revocation of licences. The Licensing Committee is only able to suspend or revoke a licence if there are reasonable grounds to believe that there has been a breach of a condition. The Licensing Committee would like to have the power to reconsider its decision to issue a licence in other circumstances, such as after becoming aware that a licence was issued on the basis of inadequate, incorrect or fraudulent information provided by the applicant.

Committee procedures and appointments

In the NHMRC submission (Submission LRC790), the Licensing Committee noted that the RIHE Act does not have any provision for the Licensing Committee to delegate a decision to the Chair, thus limiting the ability of the committee to act quickly when a rapid decision is required. Similarly, the RIHE Act makes no provision for the Chair to delegate functions or powers to a Deputy Chair. The NHMRC recommended that the RIHE Act be amended to allow such delegations.

Another significant issue identified in the NHMRC submission was the time taken to appoint replacement members to the Licensing Committee following the resignation of sitting members. This was seen to be a result of the complex requirements of the RIHE Act for making Licensing Committee appointments, and has hampered the work of the committee.

Role of HRECs

The Licensing Committee stated in the NHMRC submission (Submission LRC790) that HRECs had experienced some difficulties in understanding and performing their role with respect to consideration of licence applications. The Licensing Committee has been working with HRECs to address these difficulties.

Comments about the role of HRECs were also made by AHEC within the NHMRC submission:

> The difficulty arises because both the HREC (in compliance with the National Statement, with which it is required by the Act to function, and the ART guidelines 2004), and the LC, in compliance with the Act, must consider this question [the likelihood of significant advance in knowledge or improvement in technologies]. Difficulties arise if an HREC decides not to approve a project because it does not promise sufficient advance in knowledge, so that a necessary condition for the grant of licence by the LC is not met … This appears to subvert the apparent intention of the Act that this matter is one on which the LC ought to make the final determination. *NHMRC (Submission LRC790)*

> AHEC suggests that consideration be given to amending the legislation to make clear than an HREC review is always needed for a licence application but that the scope of that review is confined to matters of ethics of the activity. If, for example, the legislation required the LC to have regard to the advice of the HREC in reaching its decision, rather than making HREC approval a condition precedent to the grant of a licence, recurrence of the kinds of difficulties initially experienced might be avoided. *NHMRC (Submission LRC790)*

Other submissions

General support for licensing system

Several submissions complimented the NHMRC Licensing Committee for its work in issuing licences for human embryo research using excess ART embryos. Although the licensing process was described as slow and time consuming, supportive submissions considered this limitation to be outweighed by the benefits:

> The Licensing Committee carries out its role of supervision in an exemplary fashion. Although issuing licences to make hESC has been somewhat slow, we accept that the best interests of Australia was served by this approach. *Diabetes Transplant Unit, Prince of Wales Hospital, Sydney (Submission LRC180)*

> The NHMRC Embryo Research Licensing Committee has provided the Australian research community with a clear and appropriate regulatory framework to use excess assisted reproductive technology (ART) embryos. *Stem Cell Science Ltd (Submission LRC318)*

> It is AusBiotech's understanding that there has been 100% compliance with the licensing system. While there was initial feedback that the system was cumbersome and slow to respond, this has been attributed to the start up period and there is confidence that things will improve with experience and time. *AusBiotech Ltd (Submission LRC450)*

> There will be an ongoing need for future human embryo research in Australia. The current system of licensing needs to remain in place to enable IVF practices in Australia to conduct research to improve the quality of the service they provide, as well as to allow Australian researchers the opportunity to derive new and improved stem cell lines for basic research and ultimately cell-based therapies. *Stem Cell Science Ltd (Submission LRC318)*

The main overall benefits of the licensing process were identified by Stem Cell Ethics Australia as providing for:

> – general prohibitions (on grounds of safety or society attitudes) to be legislated
>
> – uniformity across the Commonwealth and states
>
> – appropriate and considered responsiveness to changes and developments in the science
>
> – some (limited) responsiveness to changes in community attitudes. *Stem Cell Ethics Australia (Submission LRC396)*

Creating and maintaining community trust in embryo research (through rigorous and transparent licensing requirements and processes) was seen as another important benefit of the current licensing system:

> The stringent requirements imposed by the Licensing Committee to demonstrate 'proper consent' and 'scientific merit' of any proposed research project prior to the granting of a licence has reassured the Australian public that any research undertaken using human embryos is fully accountable and conducted in a conscientious manner. *Stem Cell Science Ltd (Submission LRC318)*.

IVF Australia (Submission LRC346) noted that, although educational visits to research centres by the Licensing Committee and auditors were time consuming, they were beneficial to the licensing process:

> Educational visits from the members of the Licensing Committee and auditors have been very much appreciated, albeit a time consuming process. *IVF Australia (Submission LRC346)*

Shortcomings of the licensing system: inhibition of research

Problems with the licensing system ranged from minor concerns about specific issues to major concerns about the whole licensing process. A major limitation of the licensing process was identified in several submissions as the inefficient and time-consuming nature of the application and review processes. During the public hearings in Sydney, Dr Kuldip Sidhu, Chief Hospital Scientist, Diabetes Transplant Unit, Prince of Wales Hospital, Sydney, told the Committee that the licensing process was lengthy but that most researchers understood that this was because the system was new and that it would improve. He suggested that the timeframe for the application process should be about three to six months.

Professor Alan Trounson, Director of the Monash Immunology and Stem Cell Laboratories, Monash University, speaking at the Sydney hearings, agreed that the licence application took a long time but noted that he understood why this had been the case during the development of the Licensing Committee operating procedures. One problem for his research institution had been the sourcing of embryos from the IVF clinic and ensuring that proper consent had been obtained. He recommended

that both the clinic and researcher be on the licence to overcome problems with consent. This comment was consistent with the recommendation by the NHMRC (Submission LRC790) that the RIHE Act should allow joint licence applicants and licence holders.

Although other submissions also recognised that the NHMRC had required time to develop the best method of issuing and reviewing licences, several submissions noted that the lengthy time between application and approval is generally inhibitory to research. The Fertility Society of Australia (in conjunction with Monash IVF) stated:

> The aim of these Acts had been to regulate research and protect the rights of people donating embryos to research and training. Unfortunately, the lack of specificity relating to processes caused the Licensing Committee many delays over the last 3 years. As a result, delays occurred within the research arena and applicants experienced a high level of confusion and frustration. Some groups within Australia chose to cease work in view of the difficulties associated with applying for a license. *Fertility Society of Australian and Monash IVF (Submission LRC218)*

At the Adelaide hearings, Associate Professor Jeremy Thompson, Deputy Director, Research Centre for Reproductive Health, University of Adelaide, told the Committee that his embryo research laboratory, which is one of the most active laboratories in Australia, has not applied for a licence because of the restrictions and lack of support for training. In his written submission, he also noted that the licensing process is too long, too constraining and too difficult, and has slowed research:

> Within the Research Centre for Reproductive Health in South Australia, no research licence has been applied from the NHMRC to conduct research on excess human embryos. It was our opinion that internal debate about the licence process and licence activity within the NHMRC Licensing Committee required time to allow the licensing procedure to mature. There is some evidence for this, but the lengthy time between application and approval is generally inhibitory to the type of research we wish to conduct. *Associate Professor Jeremy Thompson, Deputy Director, Research Centre for Reproductive Health, University of Adelaide (Confidential submission LRC266, reproduced with permission of the author)*

Similarly, Professor John Rasko, Group Head, Gene and Stem Cell Therapy, Centenary Institute of Cancer Medicine and Cell Biology, and Royal Prince Alfred Hospital, speaking at the Sydney hearings, said that he had not applied for a licence and suggested that the process inhibits research by curbing inspiration and restricting academic freedom; however, he recognised that there were good reasons for having a licensing system because of the public's concern about the use of human embryos in research.

Shortcomings of the licensing system: inhibition of training and quality assurance activities

Some submissions included comments about applications for training licences. IVF Australia stated:

> Only one licence appears to have been granted for the training of new embryologists in some of the more invasive embryological procedures. We believe this is not because of a lack of desire to educate our embryologists but rather due to an uncertainty of how to apply for a training process. This may be an example of a process developed by the Licensing Committee in conjunction with the approved licence holder that could be simplified further and made available to other IVF units. *IVF Australia (Submission LRC346)*

Similarly, at the hearings in Melbourne, Dr Adrianne Pope, representing the Fertility Society of Australia, commented that there has been some confusion about which activities require a licence, particularly with respect to training of technicians.

Further discussion of the effect of the legislation and licensing arrangements on ART training and quality assurance activities is included in Chapter 4.

Shortcomings of the licensing system: other concerns

Several submissions expressed concern that some research on excess ART embryos was not intended to develop stem cell therapies and that, despite it being the focus of the 2002 parliamentary debate, therapeutic use of embryonic stem cells was listed as a research component in only a small number of licence applications:

> Out of the 705 embryos for which licences were given for the derivation of human embryonic stem cells, only 150 specifically mentioned using them for therapies. *Queensland Right to Life (Submission LRC376)*

> In one case the license refers to the stem cells 'eventually' being used for therapies for Parkinson's and juvenile diabetes. It is extraordinary that the Licensing Committee saw this as relevant to the application. *National Civic Council (Submission LRC246)*

The Christian Democratic Party (Western Australian Branch) questioned the granting of a licence for embryonic stem cells when the use of non-embryonic stem cells (eg adult stem cells) has been shown to have potential therapeutic applications (Submission LRC373). The National Civic Council (Submission LRC246) stated that, because there had been no successful animal models of safe and effective stem cell therapies, no licences should be issued based on the claim that stem cell lines derived from human embryos will be used for therapies:

> There is as yet no proof from animal models that embryonic stem cells can be used for safe, effective therapies for either Parkinson's, juvenile diabetes or any other condition. Until this is established then no approvals for research involving human embryos based on claims that stem cell lines derived from these human embryos will be used for therapies should be granted. *National Civic Council (Submission LRC246)*

Several submissions recommended that more specific guidelines be provided on the use of excess embryos. The Queensland Bioethics Centre (Submission LRC419) called for more stringent licensing criteria, because some of the uses of embryos (eg for training and improving ART techniques) permitted under the current licensing guidelines were not foreseen by the general community in the 2002 debate.

Using human embryos for training technicians in existing techniques was also seen by some other respondents, such as the National Civic Council (Submission LRC246), as contrary to licensing criteria (which require a significant advance in knowledge or an improvement in technology for treatment).

One of the nine licences that have been granted to date is for research on preimplantation genetic diagnosis and metabolic testing. This raised fears that preimplantation genetic diagnosis would be used by prospective parents to discard 'defective' embryos:

> Included in the nine licences granted is one for the development of methods for preimplantation genetic and metabolic evaluation of human embryos, with the obvious sequel of discarding embryos with defects regarded as being significant by prospective parents. This raises the spectre of where the line is to be drawn and what is to be regarded as a disability and whether a life is 'worthy to be lived'. *Christian Democratic Party, Western Australian Branch (Submission LRC373)*

The Committee of the St Thomas More Society suggested that the Licensing Committee's reporting to the Australian Parliament, including six-monthly reports (as required by the RIHE Act s19), had been:

> … remarkable for the sparsity of the information provided, for their lack of real analysis, and for the impression they give that investigative work is not taken sufficiently seriously. *Committee of the St Thomas More Society (Submission LRC397)*

Licence application process

Some submissions commented on different aspects of the licensing application system. One emphasised the need for the potential scientific and community benefits, and the public interest, to be considered in the application process:

> Before a licence is issued … the committee ought specifically determine that the proposal is in the public interest and that its completion is likely to achieve worthwhile scientific or other development. In considering a licence application, it ought be mandatory that the committee considers the contemplated benefits and risks of the proposal. *Committee of the St Thomas More Society (Submission LRC397)*

On the other hand, Professor Barry Rolfe, Australian National University (Submission LRC104), noted that less restrictive criteria should apply to the type and number of research groups eligible to apply for licences. Similarly, an ART researcher, Professor HW Gordon Baker (Submission LRC391) recommended that 'removal of the cumbersome licensing requirements' would help research to overcome the existing scientific limitations of ART and infertility treatment. Professor Baker suggested that research applications could be assessed adequately by institutional research and ethics committees:

> There should be an emphasis on promoting research to overcome the major continuing problems with infertility and ART. Repeal of the legislation or at least removal of the cumbersome licensing requirements would help. The institutional research and ethics committees are adequate to deal with the research applications. *Professor HW Gordon Baker, Victoria (Submission LRC391)*

Commenting further on the relationship between the assessment of the research proposal by the institutional HRECs and the Licensing Committee, Dr Adrianne Pope of the Fertility Society of Australia and Melbourne IVF (but speaking personally) expressed concern at the Melbourne hearings that the Licensing Committee had reduced the number of excess embryos available for use under their licence, compared with the number sought in their application and research protocol (which had been derived after consultation with the ethics committees at Monash IVF clinics around the country).

On the same issue, Associate Professor Malcolm Parker, a medical ethicist from the School of Medicine, University of Queensland (Submission LRC311) noted that it was unnecessary for the Licensing Committee to assess the numbers of excess ART embryos to be used for a specific project, because there would be no point in researchers using more embryos than necessary for a specific research outcome. Issues about the number of embryos could be addressed by HRECs, particularly because this requirement is already included in the NHMRC ART Guidelines 2004.

In contrast, Mr Eric Lockett, Chair of the Public Questions Taskforce, Baptist Churches of Tasmania, recommended at the Hobart hearings that the legislation specifically restrict the number of embryos produced during ART to prevent ART providers associated with embryo research from being tempted to produce extra embryos 'just to be on the safe side'.

Associate Professor Malcolm Parker also noted that the requirement that the likelihood of a proposed project achieving a significant advance in knowledge or an improvement in treatment technologies 'not achievable by alternative means' is problematic, because it is impossible for the committee to decide what could reasonably be achieved by alternative technologies. Furthermore, if it is acceptable to experiment on embryos, it should be unnecessary for scientists to justify this research in terms of alternative methods. He stated:

> This contradicts the fundamental ethos and methods of science, since both the proposed project and any alternative methodologies would need to be known in detail in order to compare them, and this presupposes too much … Funding bodies attempt to ensure that research is worthwhile, and one of the criteria for this is that the prospect of a positive outcome is not remote. There is therefore no need for the legislation to require this.
> *Associate Professor Malcolm Parker, School of Medicine, University of Queensland (Submission LRC311)*

The application process for licences has caused confusion, and some submissions cited difficulties in interpreting licensing requirements. The Fertility Society of Australia (in conjunction with Monash IVF) (Submission LRC218) stated that interpretation of the licensing requirements 'was extremely vexing for both applicants and the Licensing Committee', and the Committee of the St Thomas More Society stated that the application criteria were not sufficiently specified (Submission LRC397).

Other comments drew attention to the confusion about the types of research that the licensing system covers. The Fertility Society of Australia and Monash IVF (Submission LRC218) noted that, as new technologies and research applications are developed, it may be unclear whether current licences cover variations in a research project.

Suggestions for future operation of the licensing system

Some submissions on the operation of the licensing system were supportive of the existing structure and recommended only minor revisions, while some recommended that the system be replaced. Recommendations made by respondents about the future operation of the licensing system included expansion of the types of research that licences should allow, ongoing review of research and licence applications, and specific recommendations for changes to the licensing system.

The National Civic Council (Submission LRC246) and the Australian Family Association (ACT Branch) (Submission LRC380) recommended that no further licences be issued for the use of human embryos in training technicians in existing techniques; for creating stem cell lines (because claims of their success are premature); or for developing 'eugenic' screening tests for chromosomal abnormalities. Dr Ruth Nicholls (private citizen) (Submission LRC567) also suggested that sufficient stem cell lines are available and no new ones should be created.

The Caroline Chisholm Centre for Health Ethics Inc (Submission LRC392) identified the need for review of licence applications by experts in developmental biology and cell culture to assess whether the projects are scientifically valid. The centre noted that expert reviewers should have no conflict of interest in relation to embryonic stem cell research.

Stem Cell Ethics Australia (Submission LRC396) and AusBiotech Ltd (Submission LRC450) observed that the United Kingdom regulatory and ethical framework was a good model for appropriate legislative and ethical oversight, given 'the current stage and pace of embryonic research'. A submission by Dr Rachel Ankeny and colleagues noted that community confidence in the current licensing system could be improved through stronger accreditation and selection processes, training, and monitoring of membership of HRECs:

> While we believe that the formal regulatory structure of licensing and HREC approval in this area are appropriate, there is room to improve the operation of these processes. Community confidence in the existing licensing system and HREC review of research involving humans could be enhanced by a stronger system of accreditation of HRECs and ongoing training of HREC members… Further attention to the processes whereby ART clinics select HREC members and monitoring the balance of membership at HREC meetings would also contribute to public confidence. *Dr Rachel Ankeny, Sydney University, Associate Professor Susan Dodds, University of Wollongong, and Associate Professor Wendy Rogers, Flinders University (Submission LRC515)*

A submission on behalf of 75 third-year Bachelor of Biomedical Science students, University of Melbourne, was less supportive of the current licensing system and recommended that it be replaced by case-by-case approvals from embryo research ethics committees (under NHMRC oversight):

> We suggest that the current licensing system be replaced with a system of approval of individual research proposals by embryo research ethics committees, operating under the oversight of the NHMRC in a manner similar to current human and animal research ethics committees. Such committees have a long-standing and consistent record of ensuring that research on animals and consenting humans is conducted in an ethical manner. *Third-year Bachelor of Biomedical Science students, University of Melbourne (Submission LRC449)*

Similarly, the Australian Academy of Science (Submission LRC18) recommended that AHEC and institutional HRECs should assume responsibility for assessing the ethics of research proposals and progress and that AHEC should also be responsible for providing training and guidance.

In discussions with the Committee at the Melbourne hearings, Ms Louise Johnson, Chief Executive Officer, and Professor Jock Findlay, Chair of the Infertility Treatment Authority (Victoria), recommended that there should be more communication between the Infertility Treatment Authority, the NHMRC and the Department of Human Services (Victoria) to oversee the management of research on excess ART embryos.

Stem Cell Ethics Australia (Submission LRC396) identified 'ethical border-hopping' (where research projects are done in institutions or countries with fewer research restrictions) as a problem and suggested that a system of appropriate regulation would help to minimise this. Stem Cell Ethics Australia also stated that the benefits of research (including new therapies) should be distributed equally, and be overseen by an ethics advisory group to avoid political bias.

The Committee of the St Thomas More Society (Submission LRC397) recommended that the results of an independent evaluation of completed research projects be made public (where appropriate), along with detailed annual returns (including information about the nature of the research). They also suggested that the results of inspections by the Licensing Committee be made public in a suitable form.

9.3 Summary — licensing arrangements

The licensing arrangements under the RIHE Act are broadly supported by researchers wishing to use excess ART embryos. Delays in issuing of the first licences were accepted as an unavoidable consequence of the processes to establish the new regulatory system. However, these delays, as well as a lack of clarity in some aspects of the application process, were seen to inhibit research, training and quality assurance activities. Particularly for training and quality assurance activities in ART clinics, the system was regarded as being too cumbersome and not responsive to the requirements of these activities.

However, other respondents wanted the system to be further tightened, and some expressed concern that licences were being granted at all for training and quality assurance. The submissions showed misunderstanding about the meaning in the legislation of 'significant advances in knowledge or improvements in technology'.

The NHMRC itself has observed that there are deficiencies in the legislation relating to the operations of the Licensing Committee (including appointment of committee members, and delegation of responsibilities). There is also a lack of clarity in some aspects of the arrangements, including the follow-up of research outcomes.

10 Monitoring and compliance

10.1 Overview of monitoring and compliance arrangements

Under the RIHE Act, the Chair of the NHMRC Licensing Committee may appoint inspectors to monitor activities undertaken by licence holders to ensure compliance with the legislation. So far, the Chair has appointed one chief inspector and two inspectors. Inspectors appointed under the RIHE Act are responsible for monitoring and compliance activities under both the RIHE and the PHC Acts, although the majority of their activities relate to licences issued under the RIHE Act. They report to the Licensing Committee the findings of their activities, and these reports are included in the six-monthly reports of the Licensing Committee to parliament.

Under corresponding State and Territory legislation, each jurisdiction has agreed that the inspectors appointed under the Commonwealth legislation will also monitor compliance with the State and Territory legislation.

The monitoring and compliance framework used by the inspectors is based on a model of 'cooperative compliance', which encourages licence holders and others affected by the legislation to cooperate with the NHMRC to comply with the legislation. Emphasis is placed on education and communication to promote awareness of the responsibilities of both the licence holders and the inspectors. A key mechanism for raising awareness of the legislation is information exchange visits, which are made to researchers, licence holders, human research ethics committee members and other interested organisations. Information is also made available through seminars, workshops, websites and publications.

The inspectors monitor activities of licence holders by conducting inspections of premises, documents and records at least annually for the duration of the licence. Visits are usually arranged in advance with the licence holder, but unannounced inspections can also occur (although there has been none to date). Inspections must take place at reasonable hours. If problems with compliance are identified, the inspectors might conduct additional monitoring inspections.

Another form of inspection is the audit of records, which is conducted within a few weeks of the issue of a licence to assist new licence holders to meet the conditions of the licence relating to record keeping. At the time of expiry of the licence, a final inspection is conducted and the inspectors provide advice to the licence holder on preparation of the final report on the licensed activities.

Before or during an inspection, licence holders may request advice from the inspectors. The inspectors, under the direction of the Chair of the Licensing Committee, might also provide formal verbal or written advice to bring issues or breaches to the attention of the licence holder.

If a serious instance of noncompliance is detected during an inspection, or a formal complaint is received by the Licensing Committee, an investigation may be initiated. This may involve unannounced inspections or audits. If a breach is confirmed, actions available to the Licensing Committee include variation of the licence, suspension or revocation of the licence, or referral of the breach to the Australian Federal Police for possible criminal prosecution. Sanctions and prosecution would only be used for serious breaches where there was a clear intent by an individual or organisation to commit an offence.

10.2 Submissions and hearings

During one of its private meetings, the Committee received a briefing about the operation of the procedures for monitoring and facilitating compliance with the legislation from Mr Phillip Hoskin, Director (Chief Inspector), Compliance and Assessment Section, Centre for Compliance and Evaluation, NHMRC. During this briefing, Mr Hoskin described the standard operating procedures for monitoring and facilitating compliance. The Committee obtained further information about monitoring and compliance activities during its meeting with the Licensing Committee in Adelaide, and had access to the Licensing Committee's six-monthly reports to parliament. Written submissions and hearings also referred to the monitoring and compliance system. The remainder of this chapter summarises the information received by the Committee in these meetings, documents, written submissions and hearings.

NHMRC submission and meetings with Licensing Committee and Chief Inspector

The NHMRC submission (Submission LRC790) reported that the monitoring and compliance activities under the legislation were operating well. To date, there have been more than 30 information exchange visits to stakeholders in all States and Territories except the Northern Territory. Records audit inspections have been conducted on all licences issued, and at least one monitoring inspection has been conducted for each current licence holder. The level of compliance has been high:

> To date, with the exception of two non-compliances, all licence holders have been found to be acting in compliance with the requirements of the RIHEA and the PHCA and with the conditions of their licences. The LC also noted that all licence holders have cooperated fully with the inspectors in all inspections. *NHMRC (Submission LRC790)*

However, during its meetings with Mr Phil Hoskin, Chief Inspector under the RIHE Act, and with the Licensing Committee, the Committee heard about the limited powers of the inspectors over activities that are not covered by a licence. This issue was also raised in the NHMRC submission:

> Currently, the LC has responsibility for monitoring compliance with the PHCA, but its powers are limited if the organisation is not a licence holder. That is, NHMRC inspectors have the power to enter and inspect the premises of licence holders, but if the organisation is not licensed then entry and inspection can only be undertaken with consent from the occupiers of the premises. *NHMRC (Submission LRC790)*

As a result of this limitation, it is difficult to investigate possible breaches of the legislation by organisations that are not licence holders. For example, for a suspected breach by a non-licence holder under the PHC Act, the matter would have to be referred to the Australian Federal Police, but this could only be done on the basis of a belief, rather than a suspicion, that a breach had occurred. In contrast, other legislation (such as the Gene Technology Act) allows inspectors to obtain a monitoring warrant from a magistrate on the basis of a suspicion that a breach has occurred or is about to occur. As well, because the NHMRC inspectors have no power to enter premises of non-licence holders, the only way for them to become aware of a possible breach is if the breach is reported to the Licensing Committee.

Other submissions

Several respondents raised issues about the monitoring and inspection powers of the Licensing Committee under the RIHE Act and the system that has been put in place to implement those powers.

The existing monitoring and inspection powers of the Licensing Committee drew criticism from some respondents. The Fertility Society of Australia and Monash IVF submitted that the current monitoring and compliance requirements are suitable but are confusing. They recommended that the Licensing Committee's monitoring powers should be limited to licensed facilities:

> Monitoring and compliance requirements appear suitable but again have given rise to some confusion. The Licensing Committee's monitoring should be limited to facilities with licences only. *Fertility Society of Australia and Monash IVF (Submission LRC218)*

The Committee of the St Thomas More Society expressed serious concern about the adequacy of the Licensing Committee's investigatory processes, noting that there should be regular, random inspections to ensure that prohibited practices are not being carried out, and more detailed reporting to parliament:

> The lack of detail in the Reports to Parliament to date, and the lack of analysis, suggests a want of determination on the part of NHMRC to enforce the legislation. Given the secrecy which surrounds the ART industry generally, there is a fair possibility that abuses will not come to light at all, or at least not until disastrous consequences have arisen.
> *Committee of the St Thomas More Society (Submission LRC397)*

> Inspectors ought to conduct regular random inspections to ensure that prohibited practices are not being carried out. It is not apparent that this is happening at the present time, nor that there is a proactive approach to investigation in respect of prohibited practices. The results of those inspections ought to be publicly available in some suitable form.
> *Committee of the St Thomas More Society (Submission LRC397)*

10.3 Summary — monitoring and compliance

The processes that have been put in place for monitoring compliance with the legislation and facilitating compliance are generally regarded as suitable, although suggestions for improvements to the system were also made. It is clear that there is a major deficiency in the legislation with regard to the limited powers of the inspectors appointed under the RIHE Act to monitor activities that are not covered by a licence. As a result of this deficiency, suspected breaches by non-licence holders cannot be adequately investigated.

11 Consent arrangements

11.1 Current consent arrangements

The current guidelines for consent for the use of human tissues and reproductive materials have arisen within a context of an international consensus on the ethical practice of research with human subjects that has developed over the past 50 years, since the development of the Nuremberg Code following World War II. The 1964 World Medical Association Declaration of Helsinki provided another important set of guidelines, and further international agreements have continued to refine and specify ethical standards.

The principle of informed consent is central to ethical standards in research. This requires both the provision of information to the potential research participant and the capacity of that person to make an informed choice. Where a person is not competent to consent, a person with legal authority to decide for that participant can exercise that choice. Consent must not be subject to any coercion, or to any inducement or influence that could impair this voluntary character. A participant must be free to withdraw consent at any time.

Like many other countries, Australia has prepared statements to guide ethical research practices. These are developed by the Australian Health Ethics Committee, which is a principal committee of the NHMRC. The *National Statement on Ethical Conduct in Research involving Humans*, published by the NHMRC in 1999 (referred to here as the National Statement), [29] sets out the overall ethical principles for research involving humans and human tissues. The National Statement provides specific direction on the use of human tissue samples, including requirements for consent, and where that requirement could be waived, or waived subject to conditions. The guidelines also provide specific advice for human genetic research, including specific areas of information that should be provided to potential research participants.

The NHMRC also provides specific guidance on research involving assisted reproductive technology (ART) in the *Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research*, published by the NHMRC in 2004 (referred to here as the ART Guidelines 2004).[30] The guidelines include specific requirements for research involving gametes and research involving embryos, and emphasise that it is unethical to coerce potential research participants in any way. To ensure that these requirements are met, the guidelines state that:

> … proposals for research must include procedures to ensure that the process of providing information and obtaining consent for involvement in research is clearly separated from clinical care. (ART Guidelines 2004, paragraph 15.5)

29. See http://www.nhmrc.gov.au/publications/synopses/e35syn.htm
30. See http://www.nhmrc.gov.au/publications/synopses/e56syn.htm

Under the arrangements set out in the RIHE Act, consent to use embryos in research is a three-stage process. The first stage usually happens when embryos have been in storage at an ART clinic for some time. A letter is sent to the couple concerned to ask about their requirements for further storage. If the couple does not want to continue storage of the embryos, they can declare them to be excess. After this clinical decision has been made (that is, that the couple has completed ART treatment and has no further requirement for the embryos), the couple is asked by the clinic to nominate one of the following three options:

- donate the embryos to another couple
- allow the embryos to succumb
- donate the embryos for use in research.

If the couple chooses the research option, the embryos are moved to other storage arrangements at the clinic to await a specific request by a researcher for a research project.

Once this occurs, the researcher must obtain consent from all those responsible for the embryo, as required by the ART Guidelines 2004. At this stage, researchers must liaise with the ART clinic to contact all the persons with parental or biological responsibility for the embryo (who may be different from the ones who declared the embryo to be excess and donated it to research). This may happen some considerable time after the decision to donate an embryo to research, and is consistent with consent procedures for the use of other human material for research purposes.

Because research on the embryos will involve destruction of the embryos, the ART Guidelines 2004 require that, after the consent is signed, there should be a 14-day cooling-off period, during which consent can be revoked. The guidelines state:

> In view of the fact that once an embryo has been destroyed it cannot be restored, it is recommended that the consent of the persons responsible to a use that will damage or destroy an embryo must not be acted upon until a suitable fixed period of time for reconsideration has been allowed, normally at least two weeks after their consent to such research. This 'cooling-off' period before consent becomes effective must be explained to the persons responsible when consent is obtained. (ART Guidelines 2004, paragraph 17.17)

The legislation does not regulate the use of embryonic stem cells once they have been derived, under licence, from an excess ART embryo, including in relation to consent for further use of the stem cells. Guidance on this matter is provided by the NHMRC Australian Health Ethics Committee[31] and overseen by institutional human research ethics committees (HRECs).

11.2 Submissions and hearings

In relation to consent for donation of excess ART embryos to research, a number of ethical, motivational and operational issues were raised during the review. These are described below.

Basis of 'parental consent' for the use of embryos

Some arguments were presented that questioned the appropriate conceptualisation of consent issues. The current legislation supports the view that that those who have provided the gametes and their spouses, if any, at the time, and the woman or couple for whom the embryo was created, are the appropriate people to give consent to any research use of excess embryos. Thus, this consent is not defined in the same terms as parental consent for research with children, where consent cannot be given for research that is contrary to the child or young person's best interests.

31. See http://www.nhmrc.gov.au/ethics/human/ahec

However, some submissions made the argument that, with reference to international human rights law and other legal decisions regarding the legal rights of an unborn child (eg in relation to inheritance, and death caused by attack on the mother), human embryos should be regarded as fully human, subject to the protection of the Declaration of Human Rights, and therefore protected from research on them without their consent:

> While the law does not recognise unborn embryos as having the same rights as persons who have been born, it clearly recognises their humanity and the need to accord extra protection against deliberate or accidental harm. The provisions of the *Research Involving Human Embryos Act 2002* fly in the face of the protective culture of the law by allowing human embryos to be destroyed … *Mr Gregory E Smith, New South Wales (Submission LRC670)*

> The basis of human experimentation is *informed consent* — the NHMRC guidelines clearly state and repeatedly upholds this most basic human right (and thereby ethical benchmark). To trade-off basic human rights — to create and clone human life, experiment with this human life and then hasten death — without the prerequisite of informed consent, is to engage in the human rights abuse of slavery. *Ms Agnes-Mary Hanna, Australian Capital Territory (Submission LRC158*)

Motives for donating excess ART embryos for research

Embryo donors and other respondents to the reviews told the Committee that ART consumers regard their embryos as very highly valued material. Therefore, the decision about how to direct their use once they are 'excess' is an extremely emotional one. Many people would prefer to give them to research rather than letting them succumb, which is why the number of embryos donated for research has increased in the past few years (see Section 7.2). Once embryos have been used for research, people feel that the embryo has been of value, rather than being wasted.

For example, at the Adelaide hearings, Dr Sheryl de Lacey, an NHMRC research fellow surveying IVF patients' decisions on their excess embryos, told the Committee that 21 of the 68 people she had spoken to had discarded their embryos; approximately 17 had donated their embryos to another couple; and approximately 28 had donated their embryos to research.

She also told the Committee that many of the people she had interviewed wished to donate their embryos to research:

> … donating to research gives the middle option where they can see that they can do some benefit without a child actually coming into fruition and being an offspring that they have to consider for the rest of their lives … I've asked all of the people who have donated to research if, for example, there wasn't a research project here in Adelaide but there was one in Sydney or Melbourne would they want their embryos to go there to be used and they've all said yes. So there is a sense that they would want their embryos to be transported, or be given that option at least, so that at the end of the day they can achieve some emotional closure knowing that the embryos were actually used and were not wasted … They've got an idea that technology and research helped them to get pregnant and so they want to pay it back and they don't want their embryos to be wasted and there'll be some greater benefit. They talk mostly about the benefit being to other infertile couples and that's where they would want the benefit to go more than to the community. *Dr Sheryl de Lacey, Research Centre for Reproductive Health, University of Adelaide (Adelaide hearings)*

See Section 7.2 for more information on Dr de Lacey's research.

The consent process

The Committee heard that the separation of the initial declaration of ART embryos as 'excess ART embryos' from in-principle donation of such embryos for research purposes, and the later consent to use embryos for a specific research project, raised a number of issues. Specifically, this arrangement can increase the distress of embryo donors.

This was considered to be a particular problem when embryos donated to research are not used. In such cases, the licence holder must return the embryos to the ART clinic, or approach the donor for new consent (see Section 9.2).

At the Sydney hearings, Ms Sandra Dill, Executive Director, and Ms Debbie Jeffrey, Board Chair, ACCESS (a national organisation representing ART consumers) told the Committee that the decision to donate embryos to research is a very personal and emotional process. Therefore, it can be distressing to have the issues raised again in relation to a specific research purpose, especially when they might be raised again after a considerable lapse in time. ACCESS regarded the requirement of the Licensing Committee that the couple revisit the decision as paternalistic and proposed that the Act be amended to remove this 'onerous' requirement:

> The present bill has some provisions for additional consent which sometimes cause anxiety and distress for many consumers, and I'm referring here to a particular situation where consumers have given their consent to donate their embryos to research at some point after their treatment cycle. So they give a general consent. However when specific research is planned, those same consumers are then asked to given an additional consent to the specific procedure … Many consumers have reported to us that they find this protocol very, very uncomfortable and confronting and quite unnecessary given that they've already gone through the sometimes quite heart wrenching decision to donate their embryos to research some time ago … In reviewing this legislation, Access asks lawmakers to take a considered position based on the evidence of harm rather than opinions about perceived harm or moral objections to particular healthcare procedures specifically in the way this legislation may impact on already properly accountable clinical IVF procedures. *Ms Debbie Jeffrey, Board Chair, representing ACCESS (Australia's National Infertility Network) (Sydney hearings)*

IVF Australia also noted the difficulties of approaching people for consent to use of embryos for research when the embryos may have been in storage for possibly more than 10 years:

> We are reticent to seek second stage approval from couples where an extended time period has elapsed. Whereas some couples may appreciate the contact we believe many couples would view it as an unnecessary invasion of their lives, possibly resurrecting past disappointment and heartache. *IVF Australia (Submission LRC 346)*

Similar views were expressed by other ART providers:

> Just taking that decision to donate to research, there's an element of grieving and loss at that point even though they are surplus to their family needs. And they've made the decision with at least some anguish and to be reminded of it doesn't help them getting on with their lives. *Dr Keith Harrison, Scientific Director, Queensland Fertility Group (Brisbane hearings)*

> The current consenting process outlined by the NHMRC Licensing Committee is very cumbersome to patients. It appears that patients do not require the rigorous process outlined by the Committee. The benefits of this consenting process may need review. *Fertility Society of Australia and Monash IVF (Submission LRC218)*

This latter point was further confirmed at the Melbourne hearings by Professor Douglas Saunders and Dr Adrianne Pope (representing the Reproductive Technology Accreditation Committee and the Fertility Society of Australia, respectively), who told the Committee that by the time people need to consider the fate of their excess ART embryos, they have been in consultation with the clinic for many years and know what is involved. However, they also noted that some people may want to direct their embryos to specific areas of research.

However, other respondents did not support any change in the requirement for a two-stage consent process. Speaking at the Sydney hearings, Professor Julian Savulescu, Director, Oxford Uehiro Centre for Practical Ethics, University of Oxford, thought it important that people should not waive their right to information at both stages of consent. Associate Professor Bernadette Tobin, Director of the Plunkett Centre for Ethics, Australian Catholic University, agreed, stating that consent should not necessarily be cut back to only one stage; rather, clinicians and researchers need to find a way to inform people

truthfully and adequately about the proposed research. Dr Greg Pike, Director, Southern Cross Bioethics Institute, noted to the Committee that decision making in clinical practice should be separate from research decisions in order to avoid coercion. He noted that clinicians are often also researchers.

This raised the question of whether consent for use of human embryos should be treated in ways that are consistent with the requirements for donation of other tissues for clinical and research use, or whether there are grounds for an exception to be made for those donating embryos for ART research or stem cell research.

The obtaining of informed consent to collect and use human tissue for research purposes is expected to involve provision of full information about the research for which the tissue is to be used. These requirements are set out in the National Statement, which states that, where tissues are to be used for research that is other than that specified at the time of collection of the tissue sample, consent for the new use should be obtained. However, there is a provision in the National Statement for such consent to be waived by the institutional HREC under some circumstances (National Statement, paragraph 15.8).

To date, licences have been granted to single licence holders, even in cases where there are collaborative arrangements in place between a research institute and an ART clinic. Therefore, licences may be held by institutions other than those that hold the excess ART embryos and, at the second consent stage, there may also be a need to clarify which organisation is responsible for seeking consent and maintaining the consent forms — the organisation that holds the donated embryos, or the organisation where the research is to be done. In some situations (for example, at Sydney IVF), the stem cell research is licensed to the same organisation that was responsible for the earlier clinical care, which has an established relationship with the donors. But in other situations, the licence is held by a research organisation and the embryos are sourced from an IVF clinic. At the Melbourne hearings, Professor Alan Trounson, Director, Monash Immunology and Stem Cell Laboratories, Monash University, noted that his institution obtains embryos from the Monash IVF clinic and, as the licence holder, needs to ensure that there has been proper informed consent. To do this, the researchers need to see the consent forms, which are held by the clinic.

Chapter 4, Table 4.2 shows further information on the licences that have been granted, including joint research projects.

At the Adelaide hearings, the South Australian Department of Health and the South Australian Council on Reproductive Technology stressed that it is important to maintain full separation of decisions about clinical care from decisions about research. They did not think it appropriate for clinicians to discuss with couples the possibility of their excess embryos being used for research and would prefer this to be done by counsellors.

Consent and the purpose of research

Several respondents told the Committee that couples may wish to choose the type or purpose of the research for which their embryos are used. For example, one ART consumer commented that it is the embryo donors' decision to donate their embryos to research to help other couples in need, and that no one had the right to take this decision away (Confidential submission LRC906).

At the Melbourne hearings, Reverend Dr Colin Honey, Chair, Stem Cell Ethics Australia, stressed the importance of information about the purpose of research for which excess embryos were used. He suggested that there needs to be a distinction between basic ART research and research to develop stem cell therapies in the information provided to donors of embryos when obtaining consent for a specific research project. Professor Wayne Hall, University of Queensland, also made this point:

> … you're not just allowing an embryo to succumb if you're destroying it in the process of extracting embryonic stem cells. Those stem cells then become, if not immortal, they are going

> to continue to reproduce for a very long period of time, they are going to be used in various ways, they might lead to products that are commercialised … Clearly the consequence from the point of view of the embryo is that it's death either way, but there are consequences that flow on from the research use of embryos for the extraction of stem cells, which is different from what would happen if the embryo was simply allowed to succumb, and I think that people do need to be made aware of that. *Professor Wayne Hall, Director, Office of Public Policy and Ethics, University of Queensland (Brisbane hearings)*

This issue was also discussed in some detail when the Committee visited Sydney IVF and met researchers and members of the HREC. Sydney IVF holds four licences for human embryo research, including two for ART research and two for the derivation of embryonic stem cells. The latter licences have led to the derivation of at least one cell line. The consumer representative on the Sydney IVF HREC stressed that, in the case of research to derive embryonic stem cells, those responsible for the embryos would wish to be informed of the research (that is, through a second stage of consent) because, in this case, there may be an ongoing genetic entity (an embryonic stem cell line) derived from the embryo. Moreover, this stem cell line may be compatible with one or a number of their other children and therefore have some therapeutic potential in the future. It was suggested that people would certainly wish to know about this.

However, the consumer representative said that ART research in which there was no ongoing live genetic material after completion of the research project was a different issue, and did not require the second stage of consent.

Consent and the use of fresh embryos

The current arrangements for consent only allow the use of embryos that have been in frozen storage for research. This is because the arrangements for 'proper consent' under the NHMRC ART Guidelines 2004 require that there must be a two-week cooling-off period after consent is given for a specific research project, during which time the responsible persons involved can withdraw their consent. However, there are some situations in which it is known that embryos will never be used for reproductive purposes; for example, embryos identified by preimplantation genetic diagnosis (PGD) to be carrying genetic diseases, and embryos where other abnormalities are identified before implantation. These embryos would normally be discarded (ie they are 'excess' ART embryos).

At the Brisbane hearings, Professor John Morgan, Director of the Australian Institute of Ethics and the Professions, University of Queensland, offered the view that if researchers want to use a fresh embryo that is definitely going to be discarded (eg after PGD), there should be no need to wait for the embryo to be declared excess and then wait for a further 14-day cooling-off period. As long as arrangements are in place to avoid any coercion, prior consent should be possible (that is, consent could be given before the PGD procedure).

The same position was presented at the Sydney hearings by Professor Alan Trounson, Director, Monash Immunology and Stem Cell Laboratories, Monash University. Professor Peter Illingworth of the Licensing Committee was also of the view that the consent process outlined in NHMRC documents works well for frozen embryos but not for fresh embryos, particularly in the case of PGD.

Professor Agnes Bankier, Genetic Health Services Victoria, speaking at the Melbourne hearings, noted that in PGD all couples go through genetic counselling first and discuss what will happen to their embryos. These couples would not go through PGD unless they wanted to avoid having a child with the genetic disease. Therefore, in her view, consent obtained before the PGD procedure would not need the cooling-off period.

Consent issues for the use of eggs

Considerable concern was expressed that, if human cloning for generation of stem cells is permitted, there would be an increased demand for eggs. The basis of this concern was that the collection of eggs is a risky procedure for the woman involved, donation is associated with no promise of immediate benefit or usefulness to the donor, and efforts to increase the number of oocyte donors may inevitably lead to the coercion of donors and the commodification of oocytes. Dr John McBain, Director, Melbourne IVF, noted that only a very small number of women (3–8) have so far volunteered to be egg donors, and there would be a need to attract more donors.

At the Adelaide hearings, Dr Greg Pike, Southern Cross Bioethics Institute, Adelaide, thought that genuine informed consent would be an issue, and Associate Professor Wendy Rogers, Department of Medical Education, Flinders University also queried how women would be informed about the effects of this procedure. Others also raised this concern:

> If you're going to do this you're going to want really good eggs. You're going to need healthy eggs and so you're going to try to get them from a young woman. Now at what risk are you putting that young woman to? That's where my problem is there. *Sister Regis Mary Dunne, Mater Private Hospital (Brisbane hearings)*

The issue of payment for egg donation was also raised with the Committee. Dr John McBain thought that women who are egg donors should be reimbursed and rewarded, but also argued for the need to distinguish between payment for the service provided and for the commodity of the gamete:

> I would agree with all those who would wish to avoid gametes of any sort being seen as a commodity and I think that that is an incorrect way of looking at things. But I do believe that there is a place for rewarding the service or rewarding undergoing the inconveniencing experience of going through oocyte collection. *Dr John McBain, Director, Melbourne IVF (Melbourne hearings)*

This issue of payment for gametes (and embryos) is discussed further in Chapter 13.

A number of respondents, including Ms Katrien Devolder, Ghent University, Professor Julian Savulescu, University of Oxford, and Dr Megan Munsie, Stem Cell Sciences Ltd, noted that the need for large numbers of eggs may be a short-term issue — once there is better understanding of how cells develop, the processes currently requiring eggs may no longer be necessary. In particular, researchers are investigating the use of alternatives, such as producing oocytes from embryonic stem cells, or using embryonic stem cells themselves instead of oocytes. At the Brisbane hearings, Professor Michael Good, Director, Queensland Institute of Medical Research, outlined three potential sources of cytoplasm to 'incubate' and reprogram a nucleus, including cloned human eggs, animal eggs, and some other tissues. Further information on research in this area is contained in Section 6.2.

At the hearings in Melbourne, Ms Louise Johnson, Chief Executive Officer, and Professor Jock Findlay, Chair of the Victorian Infertility Treatment Authority, discussed the future possibility of the use of frozen ovarian tissue. Currently, quite a number of women have ovarian tissues stored as a measure to protect their fertility in the face of chemotherapy or other treatments that would damage ovarian tissue. Consent forms in these cases only cover intentions for stored tissues to form a pregnancy. If the intent of the storage could also be for nuclear transfer and embryonic stem cell research, there would need to be a different consent process.

11.3 Summary — consent arrangements

Opinions were divided on parental consent, with arguments based on the differing moral status and associated rights attributed to the embryo.

Informed consent for embryo and oocyte donation was an important issue in the public consultation process. All stages of consent were seen as having an emotional component, with many people inclined to donate excess embryos to research rather than letting them succumb.

There were three main topics relating to informed consent for embryo donation. The two-stage consent process raised most comments, with concern that the second consent stage causes unnecessary distress to embryo donors, particularly if there has been a considerable lapse of time between donation and research. Many submissions called for this second consent stage to be removed; however, others noted that some embryo donors want a say in the specific type of research their embryos are used for. In addition, the importance of the donors' right to information was seen as paramount. The question was raised whether consent for research involving human embryos should differ from the requirements of other tissue donations, particularly if cell lines will be developed for long-term use in research or development of therapies.

The use of fresh embryos raised different concerns. Some people regarded the two-week cooling-off period as unnecessary for those embryos that would be discarded (eg those identified by PGD). The suggestion was made that informed consent could be made during the education and genetic counselling process (before PGD takes place), and the two-week cooling-off requirement be removed.

The difficulties associated with attracting women to donate oocytes for research and with obtaining meaningful consent were seen as a major problem by many participants in the reviews. While some suggestions for addressing these concerns were offered to the Committee, there did not appear to be a satisfactory or generally agreed resolution to the issues raised by oocyte donation for research.

12 Oversight of ART practice and research

12.1 Introduction

As described in Sections 2.3 and 2.5, in Victoria, South Australia and Western Australia, assisted reproductive technology (ART) centres are regulated under State ART legislation as well as under the national legislation. In these jurisdictions, government agencies administer the State legislation as follows:

- Victoria — the *Infertility Act 1995* (Vic) establishes the Infertility Treatment Authority (ITA) as a statutory authority to oversee the legislative framework, which mandates licensing and reporting requirements.

- South Australia — the *Reproductive Technology (Clinical Practices) Act 1998* (SA) establishes the South Australian Council on Reproductive Technology (SACRT) as a statutory authority under the South Australian Department of Health. The SACRT has developed a Code of Ethical Clinical Practice, which has been given force as the Reproductive Technology (Code of Ethical Clinical Practice) Regulations 1995 (SA).

- Western Australia — the *Human Reproductive Technology Act 1991* (WA) imposes licensing requirements on ART providers in Western Australia. The Act is administered by the Western Australian Commissioner for Health under the Minister for Health and also establishes the Western Australian Reproductive Technology Council (WARTC) as a statutory authority to develop a Code of Practice for ART and advise the Commissioner and Minister for Health on licensing issues.

The New South Wales Health Department has undertaken public consultation on a proposed ART Bill and a finalised version of the Bill is expected to be introduced to the New South Wales Parliament in the near future. The other States and Territories have no plans to introduce specific ART legislation.

In addition to these arrangements, under the RIHE Act, the creation and use of human embryos for ART can only be carried out by an accredited ART centre, defined in the RIHE Act and current RIHE Regulations as a centre accredited by the Reproductive Technology Accreditation Committee (RTAC) of the Fertility Society of Australia (FSA). Accreditation of ART centres in Australia is administered by RTAC according to a code of practice developed by the industry (the RTAC Code 2005). RTAC is specifically included in both the Western Australian and South Australian legislation, and these States, as well as Victoria, will not issue ART clinics with a licence unless they are already RTAC accredited.

Under the RIHE Act (s9) and RIHE Regulations, research and other activities involving excess ART embryos must comply with the provisions of the NHMRC ethical guidelines for ART (the ART Guidelines 2004) to obtain ‘proper consent’ for the use of embryos. These guidelines are also mandated in the RTAC Code 2005.

12.2 Submissions and hearings

During its hearings in the States and Territories, the Committee met with representatives from the SACRT, the WARTC, the Victorian ITA, the FSA and RTAC (see Section 12.1). The Committee also received several submissions relating to regulation of ART treatment by State, Territory and national bodies.

The WARTC was broadly supportive of the framework and scope of the current legislation. However, the council noted that, in Western Australia, the broad scope of the *Human Reproductive Technology Act 1991* ensures that no use of an embryo is unregulated, and the council is playing an active role in monitoring several aspects of clinical practice that are exempt under the RIHE Act (Confidential submission LRC 410, quoted with permission of the author) (see Section 7.2).

At the Melbourne hearings, the Committee heard from Professor Douglas Saunders, Chair of RTAC, and Dr Adrianne Pope, Chair of the FSA, about the operations of RTAC in accrediting and inspecting ART units, and ensuring that these units comply with the RTAC Code 2005. Professor Saunders noted that there are currently 38 IVF units in Australia and New Zealand. He said that both RTAC and the FSA have been proactive in informing the members of the infertility community about requirements to comply with the code of conduct and with relevant state and federal legislation.

However, Dr Pope also suggested that the existence in Australia of a number of different pieces of legislation, as well as multiple guidelines and standards, had made compliance complicated because the requirements in these documents were not always consistent.

With regard to the interaction between RTAC and State statutory bodies, Ms Louise Johnson, Chief Executive Officer of the Victorian ITA, told the Committee at the Melbourne hearings that the ITA and RTAC work closely together in visiting and inspecting ART units:

> I think one of the important processes is not only is there a checking that various requirements are met in all areas of ART practice and the legislation as far as the ITA is concerned, but as well as quality assurance, quality improvement is also looked at as well. And there is quite a strong team that is put together by RTAC that visits various licensed places and clinics. We have representatives from the Infertility Treatment Authority that are involved as well and observe the RTAC practices as well as asking our own questions where they need to be asked to ensure that legislation is being complied with under the Infertility Treatment Act. *Ms Louise Johnson, representing the Victorian ITA (Melbourne hearings)*

Ms Johnson pointed to some other strengths of the current system:

> One of the positive benefits is also professional development because there's a lot of sharing of ideas and processes and practices in the various ART clinics that occur around Australia because the RTAC team is put together with representatives from all around Australia and various clinics and the role of the peer review is very strong. It's important to know that all areas of operation of the ART clinic are visited and that often personnel are questioned. *Ms Louise Johnson, representing the Victorian ITA (Melbourne hearings)*

Professor Jock Findlay, Chair of the Victorian ITA, stated at the Melbourne hearings:

> … we rely absolutely on the expertise of RTAC to give accreditation for the clinical practices of the units that we license … we're very satisfied with the RTAC process as we see it in Victoria. We think it's very thorough, very professional and we certainly rely on it for their part of it. *Professor Jock Findlay, representing the Victorian ITA (Melbourne hearings)*

Representatives of ACCESS (a national organisation representing ART consumers), were supportive of the RTAC system in their written submission and at the hearings in Sydney. A particular strength that they identified was the inclusion of a consumer representative on RTAC:

> A distinguishing strength of the RTAC model is that consumers participate as equal partners. This is unique in medicine in Australia and in ART practice worldwide … ACCESS appoints a consumer to RTAC as do the professional societies representing counsellors, nurses and scientists in addition to medical representatives. This ensures that we have access to reliable information about treatment outcomes, possible drug side effects and the quality of service provided by individual clinics. *ACCESS (Australia's National Infertility Network) (Submission LRC899)*

The self-regulatory approach of the RTAC system was seen as a benefit because of its flexibility to respond to changes in technology, among other things:

> Despite the initial scepticism of the government, RTAC has demonstrated that self-regulation can work … Benefits of self regulation include its flexibility as it is more able to respond to emerging scientific advances, reflect developing social expectations and allow for a greater degree of autonomy for consumers in the decision making process. Importantly RTAC is not restricted to rigid legislation but using the Code of Practice requirements as a minimum standard, seeks to continually improve practice. This is crucial to improving the quality of care as needs are identified. *ACCESS (Australia's National Infertility Network) (Submission LRC899)*

In contrast, the Committee of the St Thomas More Society did not support the self-regulatory approach and suggested that a legislative system for the regulation of ART practice was needed:

> The restriction of the legislation to regulation of embryo research and prohibition of practices involving use of embryos is unnecessarily restrictive. There is a need for national legislation to regulate artificial [sic] reproductive technology generally, to ensure the industry operates in accordance with established ethical standards, including transparency and full disclosure of risk. *Committee of the St Thomas More Society (Submission LRC397)*

Associate Professor Bernadette Tobin, Director of the Plunkett Centre for Ethics, claimed at the Sydney hearings and in a submission that RTAC does not monitor compliance with ethical guidelines and that this is a gap in the system:

> The Fertility Society of Australia's Reproductive Technology Accreditation Committee does not monitor compliance with ethical guidelines … Nor do individual Human Research Ethics Committees: they are too busy, and their membership is not appropriate for monitoring compliance with ethical guidelines. There is, thus, a significant gap in the arrangements for monitoring the compliance of IVF clinics with ethical guidelines. *Associate Professor Bernadette Tobin, Plunkett Centre for Ethics, Australian Catholic University (Submission LRC550)*

Submissions from State governments expressed the view that the current system for accreditation and oversight of ART units was appropriate and effective:

> The accreditation arrangements for Reproductive Medicine Units have worked effectively for South Australia for many years, and appear to be still appropriate. *South Australian Department of Health (Submission LRC576)*

> The [Western Australian Human Reproductive Technology] Act provides for the oversight of ART centres. These arrangements provide satisfactory oversight for the practice of ART in WA. *Government of Western Australia (Submission LRC782)*

> RTAC accreditation and requirements to comply with the NHMRC Ethical Guidelines provide a rigorous framework to ensure excellence in the provision of ART services. These requirements are reiterated in the Standards issued under the *Public Health Facilities Act 1999* by the CHO. There is no evidence to suggest that such accreditation and ethical oversight has been lacking or has enabled ART practitioners to engage in inappropriate practices. *Queensland Government (Submission LRC930)*

> The Victorian Government believes that the current regulatory framework, comprising both National and State bodies and the licensing regime, has successfully enforced the law and empowered responsible research that it was intended to provide for. *Government of Victoria (Submission LRC537)*

12.3 Summary — oversight of ART

Most respondents regarded the current arrangements for oversight of ART services by national and State or Territory bodies as appropriate and effective. There appears to be a cooperative relationship between RTAC, at the national level, and statutory bodies established at the State level. Advantages to the RTAC self-regulatory model include its flexibility to respond to technological change, and its inclusion of a wide range of professional and consumer interests. However, at least in some States, there may be some potential for confusion about the various requirements in legislation, guidelines and codes of conduct.

13 International exchange and trade of human reproductive materials and stem cells

13.1 Introduction

Controversy about trade and international exchange of gametes, embryos and embryonic stem cells is related to ethical concerns about the sources and uses of these materials, the commodification of human tissues, and commercialisation of any therapeutic products derived from them.

The current regulatory arrangements in Australia under the PHC Act and Customs Regulations for import and export of reproductive materials, including embryonic stem cells, are described in Section 2.4. In brief, the following arrangements apply:

- Import of human gametes (eggs and sperm) is allowed for human therapeutic use, managed by the Australian Quarantine and Inspection Service; export of gametes is not restricted.
- Import of human embryos is allowed for human therapeutic use (ie for reproductive use), managed by the Australian Quarantine and Inspection Service, but it is an offence to import a 'prohibited embryo' as defined under the PHC Act.
- Export of human embryos is regulated under the Customs Act and associated Regulations — export of 'prohibited embryos', as defined by the PHC Act, is prohibited; the Minister for Customs must approve export of assisted reproductive technology (ART) embryos, which can be for reproductive purposes only.
- Import of stem cells derived from human embryo clones or other prohibited embryos is prohibited (under the Customs Regulations); import of other stem cells is allowed (managed by the Australian Quarantine and Inspection Service).
- Export of stem cells is allowed, provided the volume of the container is less than 50 millilitres.

Transfer of gametes and embryos between States and Territories within Australia and overseas is also subject to State and Territory legislation.

Trading in human embryos (and human sperm and eggs) is prohibited in Australia under the PHC Act. This includes any inducement, discount or priority access to a service, but not payment of reasonable expenses incurred by the donor.

In the case of stem cell lines, as for other biological products with commercial potential, developers and owners of the cell lines are free to make decisions about any trade in or exchange of the products.

The remainder of this chapter provides a summary of the findings of the literature review referred by the Minister for Ageing (Biotext 2005; see Section 3.3) in these areas and a summary of comments from the submissions and hearings.

13.2 Literature review — international exchange and trade of human reproductive materials and stem cells

Import and export of human embryos and gametes

Countries other than Australia also regulate the import and export of reproductive materials. For example, both Canada and the United Kingdom require a licence from their respective regulatory authorities. In Singapore, the Human Cloning and Other Prohibited Practices Bill of September 2004

prohibits the import or export of *prohibited* embryos (those derived by cloning, or collected from the body of a woman or developed outside the body of a woman for more than 14 days). South African legislation requires ministerial approval. Italy does not permit the import or export of human gametes or embryos.

Import and export of human embryonic cells

Stem cell lines, once developed, are not reproductive material and, therefore, are not covered by arrangements for human gametes and embryos. It is difficult to establish the extent of exchange of stem cells and stem cell lines, either between countries or between laboratories within a country. This makes it difficult to be confident about the extent to which international stem cell research is using lines that have been developed in accordance with ethical standards.

A report prepared for the NHMRC Centre for Compliance and Evaluation in July 2003, *The Regulation and Use of Human Embryonic Stem Cell Lines,* considered the implications of any changes to legislation to tighten up the regulation of the use of embryonic stem cell lines, including in relation to their export. The report concluded that any move to make changes to the current regulations needs to consider whether the use of human embryonic stem cell lines poses different and additional ethical issues compared to the use of other human tissue, and whether concerns about the current Customs legislation relating to the export of small volumes apply to all human tissues, rather than only to embryonic stem cell lines.

The 2002 report of the United Kingdom's Parliamentary Select Committee on Stem Cell Research acknowledged that 'solid data on trade in stem cells or stem cell lines' were not available, but that it 'appeared that exchange of cell material was taking place on a non-commercial basis between individual scientists or research units'. The report also conceded that 'it is unlikely that official figures of available stem cell lines give the whole picture' and that there 'may be a less visible trade'.

In some countries, funding decisions provide the means to ensure that the use of embryonic stem cell lines is restricted to those derived according to ethical standards. In the United States, federal funding for stem cell research is only available for those laboratories that use a specified range of stem cell lines, all derived from excess ART embryos created before 9 August 2001. Several of the approved lines are held internationally, implying that their import as part of research funded by the National Institutes of Health would be acceptable.

In Europe, European Union funding was initially linked to embryonic stem cells derived before a particular date. This position later shifted to one permitting funding of stem cell research, but prohibiting funding of research to create embryos for the purpose of obtaining stem cells.

The Indian Government stipulates, in its *Guidelines for Stem Cell Research*, that collaboration in stem cell research will be permitted only after a memorandum of understanding and joint proposal have been approved by the Health Ministry's Screening Committee. It further stipulates that no export of cell lines as such will be permitted; however, the context implies that export in the pursuit of collaborative research would be permissible (Indian Council of Medical Research 2004).

Several countries do have some legislative oversight of international trade or exchange of stem cell lines. For example, Norway does not permit the export or import of human embryonic stem cell lines. This is consistent with its ban on creating human embryos or human embryo clones for research purposes. On the other hand, Germany permits import of embryonic stem cell lines, albeit under strict regulation, even though the creation of such lines is not permitted in Germany.

Some arrangements for the exchange of embryonic stem cells are being formalised at the nonlegislative level. For example, the UK Stem Cell Bank has formed the International Stem Cell Initiative, an international consortium of representatives of medical research funding bodies from 15 countries. This consortium has established an international program to standardise and characterise human embryonic

stem cells. The program involves the transfer of stem cells and related materials (Steering Committee of the International Stem Cell Initiative 2005). Further information on these initiatives is included in Sections 5.3 and 15.2.

International approaches to trade in reproductive materials and stem cells

Human embryos

In Australia, commercial trade in human embryos (and human sperm and eggs) is prohibited under the PHC Act. This is a position repeated in many other countries, including the United Kingdom, Canada, Singapore, Italy, the Netherlands and New Zealand.

On the other hand, an open trade in gametes for reproductive purposes in the United States includes advertising on websites.

These differences (seen also in arrangements for the donation or sale of blood) reflect two approaches to the relationship between people and their body parts and the market. While in the United States it is acceptable for some body products and parts (eg gametes and blood) to be traded commercially, European and other countries reject the commodification of the human body or the possible creation of a market that might exploit the most vulnerable. Instead, no payment may be made to the 'donor' other than to compensate for time and inconvenience.

In China, in 2002, university laboratories in major urban centres relied on rural IVF clinics for an adequate supply of human embryos. However, this created an unregulated market for embryos, with some leaders in human embryonic stem cell research stockpiling embryos to develop human embryonic stem cell lines for profit. Some foreign companies formed strategic partnerships with rural hospitals. In 2001, the Ministry of Health Medical Ethics Committee and others proposed ethical guidelines for human embryonic stem cell research that would, among other things, prohibit commercial trade in human embryos in China.[32]

Human embryonic stem cells

Legislation in a number of countries (eg Australia, Canada, Singapore, the Netherlands) prohibits trade in human gametes or embryos but is silent about the acceptability of trade in cell lines. This distinction is important because of the potential for financial benefit from patenting cell lines or associated products and processes.

In 2004, the European Group on Ethics in Science and New Technologies (an independent, pluralist and multidisciplinary body that advises the European Commission) stated that 'donors ought not to get a reward which could infringe the principle of non-commercialisation of the human body. These ethical requirements should apply as far as possible to imported stem cells.'

Under Canadian guidelines, people who agree to donate pluripotent material must be informed that the material may be exchanged with other countries and that the 'research participants will not benefit directly financially from any future commercialisation of cell lines; nor will there be any personal benefit in terms of dispositional authority over any cell lines created (ie there will be no directed donation of the cells or cell lines to particular individuals), except if the research involves autologous donation'.

32. *Ethical Guiding Principles on Human Embryonic Stem Cell Research*, Ministry of Science and Technology and the Ministry of Health, 24 December 2003

The literature review referred by the Minster of Ageing (Biotext 2005; see Section 3.3) included a summary of international views about the appropriateness of patenting embryonic stem cell lines. One view is that unmodified stem cells are not patentable; the other is that embryonic stem cells, per se, can be patentable. This discussion can be seen in Chapter 9 of the literature review.[33]

13.3 Submissions and hearings

Import and export of embryos and gametes

Reproductive purposes

There is general experience that the current export prohibitions and custom regulations regarding embryos have made it difficult for couples to export their embryos overseas for their own use:

> The embryo export prohibitions have caused ART patients wishing to export their embryos overseas for their own use, tremendous inconvenience. The process is now very slow and cumbersome and discriminatory to people wishing to have continued ART treatment overseas. This matter should be reviewed with intent to remove this prohibition. *Fertility Society of Australia and Monash IVF (Submission LRC218)*

> The introduction of Customs Regulations have made the process of embryo transportation more complex but has not appeared to have prevented couples from transporting their own gametes or embryos for their own use. *IVF Australia (Submission LRC346)*

At the Sydney hearings, Ms Sandra Dill, Executive Director, and Ms Debbie Jeffrey, Board Chair of ACCESS (a national organisation representing ART consumers), strongly argued that the current regulations for export of embryos, which involve making a personal application to the Customs Minister, are much too prescriptive and onerous. Their members who have been in this situation have found the process stressful, especially those who want to donate to another couple rather than to use the embryos themselves.

> Before 2002, they did not have to get this permission and they do not understand why they do now. There has also been a lot of misinformation about what they may be going to do with their embryos overseas (and some people have been accused of intending to sell them, which is not the case). *Ms Sandra Dill, Executive Director, and Ms Debbie Jeffrey, Board Chair, representing ACCESS (Australia's National Infertility Network) (Sydney hearings)*

ACCESS also requested that the regulation should be revoked to allow people to make their own decisions about their embryos, as was the case before 2002:

> People need to make their own decisions about their embryos. Views of parliament should not override autonomous views of potential parents [and should not] have the right to impose morality on society at large. *Ms Sandra Dill, Executive Director, and Ms Debbie Jeffrey, Board Chair, representing ACCESS (Australia's National Infertility Network Ltd) (Sydney hearings)*

The Fertility Society of Australia argued that the restrictions on the export of human embryos overseas should be lifted:

> The introduction of restrictions on the export of human embryos overseas has imposed unjustifiable inconvenience and expense to patients wishing to pursue treatment in another country. The restriction on taking embryos overseas has impacted on couples wishing to take their embryos out of Australia for the management of their own infertility, and has been cited by consumers at our own interviews as an additional invasion of their rights.
> *Fertility Society of Australia (Supplementary submission LRC218)*

33. See http://www.lockhartreview.com.au

On the other hand, the Minister for Customs, Senator the Hon Christopher Ellison, Senator for Western Australia, supported the current arrangements, which he felt to be highly desirable in principle. He informed the Committee that no delays had occurred as a result of applications to his department, that no complaints had been received and that applications had generally been processed within a short timeframe (a few days or up to a week or so, depending on the completeness of the information provided by the applicant). The minister therefore saw no reason to alter the current regulatory arrangements.

Concerns were raised that the current legislation permits export of embryos for commercial surrogacy, when such arrangements would not be permitted in Australia (Australian Federation of Right to Life Associations, Submission LRC599). This issue was also addressed by the Attorney-General's Department on behalf of Customs. They drew attention to Regulation 7 of the Customs Regulations, which only permits export for commercial surrogacy if an agreement was made or negotiations were entered into before 27 March 2003. This provision was designed to facilitate existing arrangements but will ultimately create a complete prohibition on exports for this purpose (within 1–2 years), and it may be appropriate to consider removing the 'transition' clause.

Research purposes

Support for continued limits on, or prohibition of, import and export of embryos was mentioned in a number of submissions. Most of these submissions were concerned with excess IVF embryos that will be used for purposes other than reproduction. The Diabetes Transplant Unit specifically stated:

> We accept that the exporting of spare fertilized eggs should be discouraged unless it is for the purposes of reproduction. *Diabetes Transplant Unit, Prince of Wales Hospital, Sydney (Submission LRC180)*

Other respondents were worried that, if embryos are exported, it would be difficult to ensure that trade is not involved. Similarly, there was concern about relaxation of the provisions preventing export of either embryos or embryonic stem cells:

> … as it simply commodifies human life as merely products of an industry. *Queensland Right to Life (Submission LRC376)*

Stem Cell Sciences Ltd supported the current prohibition of the import of excess IVF embryos and believed it has not affected their activities:

> Due to clear support of the couples who had excess ART embryos frozen at Melbourne IVF, the current prohibition on the importation of human embryos has not directly affected stem cell activities. *Stem Cell Sciences Ltd (Submission LRC318)*

Some respondents expressed general concern about the origins of imported embryos. One submission noted that it was difficult to see how imported embryos could be assessed to determine whether or not they had been cloned, because cloned and fertilised embryos were microscopically identical (Confidential submission LRC477).

The importance to researchers of access to imported embryos was highlighted by a stem cell research team from the Monash University:

> Suggest that the importation of embryos created by SCNT be permitted to ensure access to rare human embryonic stem cell lines (ESCC) lines [sic] of particular interest which may not be available to researchers in Australia. Furthermore, import and export of embryos will facilitate Australia's involvement in the international and global research efforts in this field by providing and having access to a sufficient number of ESCC lines for analysis. *Monash Immunology and Stem Cell Laboratories, Monash University (Supplementary submission LRC509)*

The Victorian Government noted that there would be no guarantee that embryos exported for research purposes would be used appropriately:

> The import and export of embryos should be limited to the purposes of ART treatment in accordance with the applicable infertility treatment legislation and regulatory framework. If consent were to be provided for an embryo to cross international boundaries for research, it would be difficult to monitor and enforce the use of the embryo for that purpose, and ensure it is not implanted into a womb for reproductive purposes. *Victorian Government (Submission LRC537)*

Import and export of stem cells

The legislation bans the creation, import and export of human embryo clones, but it does not regulate the import of material derived from human embryo clones (or from any embryos). However, this is covered by aspects of the Customs Act.

Several submissions argued for permitting the import and export of material other than excess ART embryos. This material includes:

- human embryonic stem cell lines
- stem cell lines derived from somatic cell nuclear transfer (SCNT) (or cloned) embryos
- fully characterised lines, as well as cells from earlier stages of stem cell derivation
- pluripotent and other human stem cells that have not been obtained by destroying ART or cloned human embryos
- cells and cell lines derived from donated excess ART embryos that have been identified as 'diseased' by preimplantation genetic diagnosis (PGD).

At the Adelaide hearings, Professor Peter Rathjen, University of Adelaide, noted that he has sourced human embryonic stem cell lines from various places, including overseas. There are many legal issues about transfer of embryonic stem cell lines, which are handled by the legal department of the university. Some cell lines cannot be imported because the methods of isolation do not meet Australian legislation. The situation will improve once the Australian Stem Cell Centre has more lines available in Australia. It is important for researchers to have access to robust stem cell lines that have been well characterised, rather than ones that behave in an idiosyncratic way.

As with imported embryos, there was concern about the derivation of imported embryonic stem cell lines. For example, the NHMRC acknowledges that:

> At the time the legislation was developed it was considered unacceptable that Australian scientists should be able to freely import embryonic stem cell lines derived from an embryo that was created via a process that would be banned in Australia (such as SCNT). *NHMRC (Submission LRC790)*

Stem Cell Sciences Ltd noted:

> International exchange of embryonic stem cell lines must be permitted provided such cell lines have been derived using practices consistent with Australian legislation and those of the exchanging nation. *Stem Cell Sciences Ltd (Submission LRC318)*

While agreeing that imported cell lines should have been generated in accordance with Australian legislation and standards, the Diabetes Transplant Unit, Sydney (Submission LRC180) saw no reason why the import of cell lines should be the subject of legislation. The unit argued that existing quarantine laws adequately cover the international exchange of human embryonic stem cell lines. This was also considered as a possible option by the NHMRC (Submission LRC790) and Stem Cell Sciences Ltd (Submission LRC318).

The Victorian Government's submission emphasised the importance of free exchange of stem cell lines for Australian and international research:

> Given that the number of stem cell lines available internationally is extremely limited, the import and export of embryonic stem cell lines is a very important issue for researchers. Providing access to lines developed overseas is critical for extending Australian research. Similarly, Australian researchers are committed to developing the field internationally by providing Australian derived and developed stem cells to international counterparts … If undue limitations are placed on the movements of lines, it will limit Australia's capacity to participate in international projects and thus impede efforts to develop an international approach to the development of this field. *Victorian Government (Submission LRC537)*

Other submissions also argued that allowing the free exchange of human embryonic cell lines would minimise the number of human embryos used to generate embryonic stem cell lines overall, while numerous others considered it to be essential for research in this field to continue.

In their submission, the NHMRC accepted that the creation of human embryo clones for research is a recent development and has led to rapid scientific advance in other countries, such as the United Kingdom and South Korea, and recommended that:

> The LRC may wish to consider the implications of potential future benefits, if any, from the use of embryonic stem cells derived from cloned human embryos in research, and the value of retaining the prohibition on the import of viable products derived from human embryo clones *NHMRC (Submission LRC790)*

In addition, a number of groups requested that the Committee consider permitting the import of human embryonic stem cell lines derived from SCNT, even if SCNT was not permitted in Australia. This would mirror the current situation in Germany, but would be at odds with the accepted view that embryos created by methods that are prohibited in Australia should not be imported:

> The continued prohibition on importing stem cells derived from prohibited embryos (eg nuclear transfer progenitors) together with the prohibition on creation of nuclear transfer progenitors, ensures that Australian scientists who choose to remain here are prevented from participating in a fundamental line of research that potentially carries huge social and economic benefits for all Australians … the Legislative Review Committee should recommend the amendment of the *Prohibition of Human Cloning Act 2002* and the Customs (Prohibited Exports) Regulations 1956, to allow the importation of stem cell lines derived from nuclear transfer from appropriately regulated 'approved' international Stem Cell Banks. *AusBiotech Ltd (Submission LRC450)*

> We do not see the need for a prohibition on importation and exportation of cloned embryos, as is contained in Section 11 of the Act. The exchange of information and materials between laboratories is the lifeblood of science, and is essential in order for experiments to be replicated. A refusal to accept and participate in the advances of international science will only serve to leave Australia in a state of technological isolation. *Third-year Bachelor of Biomedical Science students, University of Melbourne (Submission LRC449)*

Commodification of gametes and embryos

The Committee heard considerable support for the continuation of the ban on payments for human embryos and gametes. The argument made to the Committee in support of the current position was that it is important to avoid the commodification of human life, or the exploitation of women (for whom the donation of gametes is most risky). At the Melbourne hearings, Professor Louis Waller, Monash Law, Monash University, pointed out that:

> [Commercialisation and commodification are for me] a very serious concern. I think those two unruly horses fame and fortune can drag particular people in directions which are not in the public interest and these are issues that have to be very carefully addressed … Talking about the buying and selling not just of human beings but of the parts of human beings even if those parts are very small should remind us that we are what we are and buying and selling in that

> regard should never be accepted — never be countenanced. *Professor Louis Waller, Monash Law, Monash University (Melbourne hearings)*

Some submissions and a number of comments in the hearings were in favour of the prohibition of payment for gametes and embryos, and a few submissions supported payment beyond reimbursement of reasonable expenses. However, the result of the current prohibition was perceived differently by different groups. Stem Cell Sciences Ltd (Submission LRC318) said the legislation has not affected its access to embryos, whereas the Christian Democratic Party, Western Australian Branch (Submission LRC373) believes the prohibition has effectively restricted access.

AusBiotech supported continuing the policy of prohibiting payment for gametes and embryos, but also noted:

> … we believe it is worth exploring other means of accessing donor eggs — particularly if the prohibition on creation of nuclear transfer progenitors is lifted … AusBiotech would support a proposal to assess whether the current organ donation model to donate ovarian tissue would be an appropriate vehicle for consenting women to list their eggs for donation. *AusBiotech Ltd (Submission LRC450)*

The Committee of the St Thomas More Society recommended that appropriate amendments be made to the legislation to ensure that activities involving the commercial trading of human eggs, sperm or embryos cannot occur offshore. The council noted that the Licensing Committee report to the government for the period 1 April 2005 – 30 September 2004 contained an account of an investigation into commercial trading in human sperm. However, while the report:

> does not say precisely what was the basis of the Director of Public Prosecution's advice, it would seem that the legislation is being avoided by operating, at least in part, off-shore. If this is the case, it is appropriate that there be amendments to the legislation to ensure that the legislation is not avoided in this fashion. *Committee of the St Thomas More Society (Submission LRC397)*

At the Adelaide hearings, Dr Sheryl de Lacey, Research Centre for Reproductive Health, University of Adelaide, reported that, in a survey of people with excess ART embryos, people did not indicate that they wanted any payment. However, they mentioned the amount of effort and cost that has gone into creating and storing embryos ($200 per year for storage alone). People should not be out of pocket for these expenses. In terms of donation of oocytes, there are more risks to the donor than for donation of embryos. However, people do not necessarily want a cheque in the mail but would like to see some benefit coming from their donation.

Speaking at the Melbourne hearings, Dr John McBain, Director, Melbourne IVF, thought that women who are oocyte donors should possibly be rewarded. However, he stressed that it would be important to distinguish between payment for the service provided and payment for the commodity of the gamete. Paying for the service would not involve commodification of human tissue.

Speaking at the Sydney hearings, Professor Julian Savulescu, Director, Oxford Uehiro Centre for Practical Ethics, University of Oxford, pursued this argument much further:

> … I think that we should permit trading in tissue and organs including gametes and embryos and the real ethical issue is setting a fair price to avoid exploitative arrangements … Now this idea of altruistic donation is a complex one. In many cases it's not altruistic. People that donate kidneys altruistically are often doing it because they're coerced by family members. In the case of eggs it may be other families who have sick relatives that they think are going to benefit from this sort of science will be putting coercion on them. I think a very viable alternative is to set a fair price for the embryos and then it's clear the person is doing it because they judge that the money outweighs the risks. So I think that's more contentious and I think we need to see whether we really need to move to paying egg donors.
> *Professor Julian Savulescu, Director, Oxford Uehiro Centre for Practical Ethics, University of Oxford (Sydney hearings)*

However, other respondents said that the current prohibitions ensure that exploitation of women donating eggs is avoided. For example, the Christian Democratic Party (Western Australian Branch) said:

> … we applaud this prohibition. To allow such payment would be to facilitate the exploitation of women to provide eggs and to commercialise and therefore trivialise human life.
> *Christian Democratic Party, Western Australian Branch (Submission LRC373)*

At the Adelaide hearings, Dr Greg Pike, representing the Southern Cross Bioethics Institute, said that commodification of human life has the potential for coercion, and that the institute would not endorse any payment of donors.

See further discussion on consent for the donation of eggs in Chapters 6 and 11.

13.4 Summary — international exchange and trade of reproductive materials and stem cells

Controversy about trade and international exchange of gametes, embryos and embryonic stem cells is related to the impact of regulatory requirements on couples seeking to export embryos for their own reproductive use, ethical concerns about the sources and uses of these reproductive materials, the commodification of human tissues, and commercialisation of any therapeutic products derived from them.

There appeared to be general agreement that the current export prohibitions and Customs regulations regarding embryos have made it difficult for couples to export their embryos overseas for their own reproductive use. However, there was less consensus about the impact of Customs regulations on research. Some researchers were of the view that the current import and export restrictions on embryos were not affecting their research, whereas others noted the importance of Australian researchers having access to embryonic stem cells from overseas.

The current legislation bans the creation, import and export of human embryo clones, but it does not regulate the import of material derived from human embryo clones (or from any embryos) such as embryonic stem cell lines, which is covered by aspects of the Customs Act. There was general concern about whether such imported cell lines have been derived using practices consistent with Australian legislation.

There is a strong view that gametes and embryos should not be commodified by permitting their sale. Respondents were also concerned to see the benefits of altruistic donation translated into public benefit and access to therapeutic applications arising from the research (see Chapter 14).

14 Biotechnology and commercialisation

14.1 Introduction

It is likely that research using human embryos will only be translated into widely available clinical products and processes if the results of the research are commercialised. The commercialisation process requires investment, either public or private, and protection (through patents) of intellectual property arising from the research. This process, including the long lead times for conversion of research to therapies, and the need for commercialisation of research results are not well understood by the general public.

Australia has a strong research base in human stem cell research. Australian scientists, backed by both public and private funding, have established several companies and organisations that are capable of commercial development of research outcomes. In relation to these reviews, it is of note that recent media reports, such as in *The Australian* ('States to attack ban on cloning', 21 November, 2005), have highlighted the importance of stem cell research to the Australian biotechnology industry and the concern of several State government ministers that the current prohibition on somatic cell nuclear transfer (SCNT) in Australia would lead to the drift of scientific expertise to countries where such research is permitted.

During the review, the Committee received a large number of submissions and comments relating to commercial use of products and knowledge arising from human embryo research. These are summarised in the remainder of this chapter.

14.2 Submissions and hearings

Economic and intellectual benefits of human embryo research to Australia

As indicated in Chapter 6, the Committee received numerous submissions from researchers, research organisations, State governments, patient groups and individuals highlighting the potential importance of stem cell research to Australian industry.

The Committee was made aware that, historically, Australian researchers and assisted reproductive technology (ART) practitioners have been world leaders in the development of ART and embryonic stem cell research. However, in the past few years, while Australia has prohibited certain types of embryonic stem cell research (specifically SCNT), several other countries (including the United Kingdom, Singapore, South Korea, and some states of the United States) have permitted such research.

Some of the potential consequences of this disparity between Australian laws and those in other countries have been addressed in Section 6.3, where the disadvantage to Australian researchers and the possibility of restricted access to new therapies were highlighted. From an industry perspective, the Committee was told that some of Australia's researchers may choose to move to countries where their research is more actively supported. This 'brain drain' would result in loss of intellectual capital and expertise from Australia:

> [As a result of the ban on SCNT] Australia will continue to lose its position as a world leader in this field of research together with its leading scientists (a recent review of international stem cell research in the *National Geographic* mentioned Australia only once and that was to comment on the loss of scientists to Singapore). *AusBiotech Ltd (Submission LRC450)*

> The Australian community (and in the longer term, the international community) is also disadvantaged by not having timely access to experimental therapies through clinical trials

> process and more broadly through the loss of intellectual and creative capital as researchers (and research investment) move off shore. *AusBiotech Ltd (Submission LRC450)*

> Therapeutic cloning is permitted in numerous modern countries, so the Australian ban will have little long-term effect on the development and use of such procedures. However our ban does severely restrict the activities of Australian researchers, or requires them to move their work overseas — which is generally seen as an undesirable situation and part of the 'brain drain'. When such therapies become commonplace, as seems certain, the current Australian legislation would force people to have their treatment performed overseas. *Dr Andrew Fry, Victoria (Submission LRC401)*

> Australia is likely to suffer a loss of top-class researchers if the constraints of the current legislation are not eased. Several senior scientists in the field have already indicated that they will seek opportunities overseas if there is no easing of the restrictions on the use of human embryos in research. In addition, there are likely to the huge financial rewards in the future for those countries developing stem cell therapies. Retaining the restrictive legislation is likely, therefore, to lead to loss of the massive revenue for Australia and to an erosion of our world class research base. *Dr Peter Williamson, Western Australia (Submission LRC413)*

Although the international nature of information about research and technology means that it is not imperative that the research is done in Australia, a 'brain drain' may restrict the economic development of Australian research and biotechnology, including investment in Australian research:

> If Australian academic and commercial scientists are prevented from pursuing this important line of stem cell research, not only will Australian scientists be forced to surrender their leading position in the field to scientists from countries with more supportive legislation, but Australia will fail to develop and directly benefit from the ensuing biotechnology industry. *Stem Cell Sciences Ltd (Submission LRC318)*

> The comparatively restrictive legislative environment combined with the potential for loss of leading researchers does not provide the certainty required to make Australian research an attractive investment opportunity for either private Australian or international investors. The obvious consequence of this is either a greater call on the public purse or a decline in the quantity or quality of the research being undertaken in this field in this country. *AusBiotech Ltd (Submission LRC450)*

Similar views were expressed by several State governments in their submissions to the Committee:

> The current ban hampers science and therefore the economic potential for this research, as our international competitors (eg the UK, Singapore) are currently taking the lead. *Queensland Government (Submission LRC930)*

> Allowing SCNT as described above for generation of embryonic stem cells under strict guidelines would enable Australian scientists to participate in this promising research and to maintain their internationally competitive edge … Should the present Australian prohibition on SCNT research be maintained after 2005, Australian stem cell research competitiveness would be eroded. *Victorian Government (Submission LRC537)*

> At this point, Australia is one of the few countries with advanced biomedical research capacity that prohibits SCNT. The technique is not illegal in the United Kingdom, the United States, South Korea, Israel or Singapore. The regulatory regime in places such as the United Kingdom has allowed all types of stem cell research and particularly embryonic stem cell research to flourish … This research will proceed irrespective of Australia's position. It would be profoundly unfortunate if the strength of Australian research and the benefits to the community were foregone through continued prohibition against this technique. *New South Wales Ministry for Science and Medical Research (Submission LRC1016)*

The Committee also heard that restriction of Australian research could have other direct economic impacts, since Australia will have to buy the results of successful research from other countries. For example, in response to a query from the Committee about the consequences of Australia not pursuing embryonic stem cell research, Professor Alan Trounson, Director, Monash Immunology and Stem Cell Laboratories, speaking at the Sydney hearings, stated:

> It will be done somewhere else, essentially. If we don't do it in Australia there are so many other countries doing it that we will just get it back as a technology and pay for it appropriately … So I think if you don't do it you will miss out. We will only miss out for a certain period of time because medicine will buy the reagents and the materials and expertise from overseas to help our patients eventually, but in the meantime we would have missed out substantially. *Professor Alan Trounson, Director, Monash Immunology and Stem Cell Laboratories (Sydney hearings)*

On a similar theme, Professor Suzanne Corey, representing the Australian Academy of Science, stated at the Melbourne hearings that Australia can only expect to derive benefits from international research if it participates in that research:

> You cannot expect sharing of information and sharing of the agents, sharing of materials, full participation in the global effort unless you are willing also to expend your own energy, your own money … Countries that do not have their own sophisticated research endeavour are unable to even fully avail themselves of advancements that are made overseas. They're unable because they don't have the framework of professional expertise that allows them to sift through the many things on offer and acquire the most appropriate for their community and they don't have the wherewithal to be able to afford to bring those things in because they have not actually contributed to the whole endeavour. *Professor Suzanne Corey, representing the Australian Academy of Science (Melbourne hearings)*

Professor Bob Williamson, also representing the Australian Academy of Science, told the Committee at the Melbourne hearings that a 'brain drain' could result in research moving out of the public sector in Australia, with a loss of accountability and openness of research:

> If this research is over restricted in one of the countries that has been a paradigm for public research and public/private partnerships — which Australia has been for many years — all it will mean is that our best genetic scientists go to the States, which has a different model, go to Singapore which has a different model, and I think that will be very much to the disadvantage not only of Australia which it undoubtedly will be, but also to those of us who believe in openness, in accountability and in appropriate regulation of research. Then it will be moved out of the public sector. *Professor Bob Williamson, representing the Australian Academy of Science (Melbourne hearings)*

Other attitudes to commercialisation

In contrast to many of the views expressed above about the commercial importance of human embryo research, other submissions drew attention to concerns about the commercial use and development of therapies resulting from such research.

One view expressed was that ethical concerns are of greater importance than commercial considerations and should take precedence in decisions about whether certain types of research should be permitted:

> Arguments that Australia will be left behind in research or that we will lose scientists and/or export income if we do not lift the ban should not be allowed to overshadow the ethical arguments against human cloning. *Graham and Joanne Russell, New South Wales (Submission LRC27)*

> The Committee will hear that Australia must not fall behind, that investment opportunities must not be lost, that such research is inevitable and that Australia must join the rush. But the Committee need not be swayed by this debased 'leaders and followers' rhetoric. Good science is not that which makes the most money, or panders to consumerism, or makes our medical researchers into merchants and commodities traders; and so Australia may choose to be different. *Anglican Church of Australia, Sydney Diocese (Submission LRC780)*

Other comments to the Committee about commercialisation of research were based on the assumption that gametes and embryos used in developing the commercial product are donated altruistically (see Chapter 13). While altruistic donation avoids the commodification of life at the stage of donation of tissue, commercial and therapeutic benefits may emerge over time. People are concerned that these benefits and profits remain in the public domain, through public ownership, and that therapies remain available within the public health system.

For example, a submission from Dr Rachel Ankeny and colleagues argued:

> We believe that the products and profits from the research involving SCNT and the development of stem cell lines including a stem cell bank (should they proceed in Australia) should remain in public control, and equally available within the public healthcare system. The current climate of competition between the states for commercial biotechnology investment raises concerns that there will not be public ownership of many resources donated by Australian women for stem cell research. *Dr Rachel Ankeny, Sydney University, Associate Professor Susan Dodds, University of Wollongong, and Associate Professor Wendy Rogers, Flinders University (Submission LRC515)*

Mr Adam Johnston suggested that ownership of tissues donated for research was important and that consideration should be given to granting donors some form of rights in the benefits of the research:

> There is another very serious matter of property rights, patent law and what this could mean for public access to the therapeutic benefits of stem cell technology … as we are dealing with things so intimate and personal to each living human being, jurists and policy makers must not only acknowledge the legal rights of patent holders but also the equitable rights of those who provide samples. *Mr Adam Johnston, New South Wales (Submission LRC287)*

Stem Cell Ethics Australia (Submission LRC396) stated that there would be significant community benefit if a nationally owned drug company were formed to ensure some public control of research results.

At the Adelaide hearings, Associate Professor Wendy Rogers, speaking as an individual, discussed the commercialisation of research outcomes. She stressed that she is opposed to a market in human tissue in any form. However, if products with commercial potential are developed from altruistic donations, equity considerations mean that there should be mechanisms in place to ensure that the products remain at least partly in the public domain rather than moving entirely into private profit:

> I think there is a serious equity issue when tissues that are donated by Australians for scientific research … then can be used to develop commercial products … We're going to have a net movement of tissue that's donated by the Australian public into research which then may end up with products that are patented to create profits for private industry and products that are marketed, and then access to those might be governed by financial resources … I would like to ensure that altruistic donation is still the norm in Australia, but that that gift that those women make in this situation is protected and that the profits go back into the public sector and into healthcare that is available to all women rather than into the private sector. *Associate Professor Wendy Rogers, Department of Medical Education, Flinders University (Adelaide hearings)*

Associate Professor Rogers noted that consent issues are also crucial:

> I think it's imperative that health ethics committees that are approving this kind of research should ensure that all efforts are made to make sure that the women are fully informed about the possible uses of the oocytes and the fact that they have no control once they've donated the eggs for research, no control over the kinds of research and no control over the profits and no share in the profits. *Associate Professor Wendy Rogers, Department of Medical Education, Flinders University (Adelaide hearings)*

14.3 Summary — biotechnology and commercialisation

Strong arguments were put to the Committee that there would be benefits to the Australian biotechnology industry and the Australian economy from the types of research that are the subject of the Acts. There was widespread speculation that a legislative environment restricting the types of research that could be done in Australia could lead to a 'brain drain' of Australian scientists to other countries where such research is permitted. This was seen as a particular issue for the technique of SCNT, which is prohibited in Australia but permitted in a number of other developed countries. Loss of Australian scientists would have implications for Australia's research base, biotechnology industries and economy, as well as potentially restricting the access of Australians to benefits of the research.

A number of submissions noted that there should be mechanisms to ensure that donors and other members of the public have access to the benefits of research and that social justice issues should be of concern at all stages of the stem cell research endeavour. While the majority of participants acknowledged such concerns, industry groups and researchers emphasised that commercialisation is an essential aspect of research and development in this area and that, without investment, new therapeutic products cannot be developed.

15 Applicability of establishing a national stem cell bank

15.1 Introduction

As the number of human stem cell lines has increased throughout the world, it has become apparent that there is a need for the creation of stem cell registries and stem cell banks to enable researchers to locate cell lines of interest, along with appropriate information about source and quality. While the current focus of interest in stem cell banks is on the registration and storage of embryonic stem cell lines for research, it is possible that in subsequent years advances in stem cell engineering and transplant immunology may mean that stem cell banks also come to fulfil an important clinical function.

This chapter presents information on stem cell registries and banks from the literature review referred by the Minister for Ageing (Biotext 2005; see Section 3.3),[34] and a summary of information from the submission and hearings.

15.2 Literature review — international stem cell registries and banks

Stem cell registries

Stem cell registries hold information about the source, characteristics and derivation of stem cell lines. A number of registries and initiatives to establish registries are currently active.

In the United States, the National Institutes for Health (NIH) Human Embryonic Stem Cell Registry lists the derivations of stem cells that are eligible for federal funding. The registry provides contact information to facilitate investigators' acquisition of stem cells, and a unique NIH code for each cell line. Researchers must use the code when applying for NIH funding.

In January 2003, the United Kingdom's Medical Research Council brought together nine international research agencies that had indicated an interest in working together to further stem cell research. The International Stem Cell Forum[35] now has 16 members: Australia, Canada, the Czech Republic, Denmark, France, Germany, Finland, Israel, Japan, the Netherlands, Singapore, Sweden, Switzerland, the United Kingdom, the United States, and the Juvenile Diabetes Research Foundation. Seventeen laboratories from 11 forum member countries are contributing 75 human embryonic stem cell lines to a collaborative set of characterisation studies. The United Kingdom's Stem Cell Bank is the hub for collection and distribution of materials. This project is regarded as a pilot phase of the International Stem Cell Initiative that will lead to formal mechanisms for large-scale international collaboration.[36]

In June 2005, the Canadian Institute for Health Research published its *Updated Guidelines for Human Pluripotent Stem Cell Research*. The institute announced its intention to establish an electronically accessible national registry of human embryonic stem cell lines generated in Canada. The registry is intended to minimise the need to generate large numbers of cell lines, and thus reduce the need for large numbers of donated embryos. All human embryonic stem cell lines generated using the institute's

34. See http://www.lockhartreview.com.au
35. See http://www.stemcellforum.org
36. Steering Committee of the International Stem Cell Initiative (2005)

funds will be listed with the registry and must be shared with other researchers 'subject to reasonable cost-recovery charges'. Participation in the registry will be a prerequisite for obtaining institute funding for human pluripotent stem cell research.

Currently, the International Society for Stem Cell Research also maintains a web-published registry of cell lines that are not eligible for NIH funding, as well as additional information and protocols. The June 2005 listing carried information on lines from several public and private agencies.[37]

Stem cell banks

United Kingdom Stem Cell Bank

The United Kingdom Stem Cell Bank at the National Institute for Biological Standards and Control in Hertfordshire began operating officially in January 2003. The bank, which is funded by the United Kingdom Medical Research Council (75%) and Biotechnology and Biological Sciences Research Council (25%), will 'curate ethically sourced, quality controlled adult, fetal and embryonic stem cell lines and will be open to academics and industrialists from the United Kingdom and overseas'. The bank is a repository for stem cells (adult, fetal and embryonic), and provides cell lines for basic research and clinical applications.

The bank is governed by a steering committee and codes of practice for management and for the use and deposit of, and access to, stem cell lines.[38] A local management committee of the National Institute for Biological Standards and Control reports to the steering committee. User and clinical liaison committees have been established to provide forums for debate and consultation.

The aims of the bank are to create, grow and supply well-characterised stem cell lines for use in research in the United Kingdom and internationally, and to deliver cell lines for use in the production of therapeutic materials.[39] The bank handles and stores cells using 'good manufacturing practice' that meets requirements for human medicines, so that they are suitable for therapeutic purposes.

The bank's code of practice, developed by its steering committee, encourages deposition of stem cell lines according to specifications for practical, regulatory, quality, risk management, safety and legal requirements to comply with national and international legislation and fulfil the bank's aims. The code takes into account donor selection, ethical issues, accreditations and authorisations, information and consent.

The bank does not become involved in intellectual property negotiations between depositors and users of lines. Its charges range from marginal cost recovery for academic researchers to full cost recovery for commercial users. Requests for permission to obtain cell lines must be made to the steering committee on the application form obtainable from the bank's website. Applications to deposit a cell line follow the same process.[40]

United States national embryonic stem cell bank

In July 2004, the United States National Institutes of Health announced plans to develop a national embryonic stem cell bank to consolidate some of the available embryonic cell lines into one location.[41] The grant to operate the bank is expected to be awarded in late 2005.

37. See http://www.isscr.org/science/sclines.htm
38. See http://www.mrc.ac.uk/index/strategy-strategy/strategy-science_strategy/strategy-strategy_implementation/strategy-government_spending_review_initiatives/strategy-stem_cells/strategy-stem_cell_governance.htm
39. See http://www.mrc.ac.uk/txt/index/strategy-strategy/strategy-science_strategy/strategy-strategy_implementation/strategy-government_spending_review_initiatives/strategy-stem_cells.htm
40. See http://www.ukstemcellbank.org.uk/Research.html
41. See http://msnbc.msn.com/id/8061078/

In the tender documentation[42] for contractors to establish the bank, its stated purpose is to:

> … perform in-depth characterization and comparison of all approved hESC lines and subclones derived from them, and with the agreement of the owners of hESC lines to maintain, produce and distribute these cell lines and subclones to the research community … If the activities of the NSCB are performed at more than one institution, there must minimally be a single electronic portal (eg a web site) through which any party outside of the NSCB can access all of the data derived by the NSCB, obtain all required customer service functions and through which those outside parties can obtain all of the hESC lines that are available through the NSCB. In summary, the NSCB should greatly facilitate the investigation of the functional diversity of the approved hESC lines, leading to specific opportunities for translational research.

Other stem cell banks

Sweden's National Stem Cell Bank was created before the United Kingdom bank. Funding for three years from the Swedish National Research Council was granted in 2002. Sweden is involved in the International Stem Cell Forum and the forum's registry.

The Chinese Government approved the setting up of a national stem cell bank in 2002.

Plans for a 'world stem cell bank' in South Korea in the near future were reported in May 2005. This bank will provide consolidated stem cell lines, some originating from human embryos, cloned for research.

There are also press reports that the United Arab Emirates Department of Health and Medical Services is creating a stem cell bank, although details are not provided.

Source information on these stem cell banks is provided in the literature review (Biotext 2005).[43]

15.3 Submissions and hearings

Overall support for a national stem cell bank

Support for a national stem cell bank was given in many written and oral submissions. Some comments gave general support to a stem cell bank, while others were more specific about the inclusion of embryonic stem cell lines and the availability of all cell lines stored within the bank to the research community.

For example, AusBiotech supported stem cell banks in general because:

> They ensure that cell lines are produced and maintained to an internationally recognised standard; the history of the cell lines and their derivation is transparent; they ensure the most efficient use of embryos (and in the case of nuclear transfer technology, eggs) by minimising the opportunity for repetitive work by researchers; and they reduce the overall cost of research *AusBiotech Ltd (Submission LRC450)*

The Queensland Government emphasised the potential benefits of a stem cell bank to international research collaborations, as well as a number of other benefits:

> The collaborative nature of international research suggests that a central repository of stem cell lines and information may enhance research outcomes and capacity. A national central bank may be able to form links with other stem cell banks internationally and expand the lines available to Australian researchers. An Australian bank may provide a level of public scrutiny over the number and types of stem cell lines in existence and the level of research being undertaken. The United Kingdom stem cell bank at the National Institute for Biological

42. See http://www.ukstemcellbank.org.uk/Request.html
43. See http://www.lockhartreview.com.au

> Standards and Control indicates that the national stem cell bank will also reduce the number of excess ART embryos needed by researchers, as access will already be available to stem cell lines the researcher may otherwise have had to create. A national stem cell bank may also provide a link into the administration of therapeutic goods to ensure that therapies ultimately devised from stem cell lines are of an acceptable quality for human use. *Queensland Government (Submission LRC930)*

The Victorian Government recommended that a national stem cell bank build on the major national research facility at the Australian Stem Cell Centre, which is already capable of storing stem cell lines (Submission LRC537). In addition, the Western Australian Government noted the need for a stem cell bank to take advice from other jurisdictions, as well as ethical legal issues and the potential community benefits (Submission LRC782).

Conditional support for a national stem cell bank was given in some written submissions, provided the bank excluded embryonic stem cells. Three of these submissions recommended that the bank also include cord blood. For example, the Christian Democratic Party (Western Australian Branch) said:

> We would be totally opposed to a bank with ES cells but a national non-ES cell bank eg using cord blood stem cells, would be ethical and in line with similar banks for blood and marrow products. As well as being a therapeutic resource it would facilitate research in different institutions that otherwise might have difficulty in accessing stem cells. *Christian Democratic Party, Western Australian Branch (Submission LRC373)*

The issue of a cord blood bank was also raised by other respondents:

> As grandparents of a 650g birth weight premature baby who has chronic lung disease … we have often wondered whether our grandson's cord blood could have been used to produce stem cells to cure his lungs. This leads to the question: would it be beneficial in the long run, to set up a cord blood bank for each baby born? *Mr George and Mrs Maureen Wright, New South Wales (Submission LRC97)*

At an informal meeting with the Aboriginal Medical Services Alliance in Darwin, the Committee heard that the issue of blood and body parts and blood tissue is highly controversial for Indigenous communities. This has been highlighted by the Human Genome Project, and there has been ongoing concern and debate about the ethics involved in the collection, storage and use of human samples.

At the Melbourne hearings, Professor Bob Williamson, speaking on behalf of the Australian Academy of Science, said that the Academy did not have a specific view on the establishment of a national stem cell bank, but would like to see an international stem cell bank.

Advantages of a national stem cell bank in Australia

Written and oral submissions identified three main advantages of an Australian national stem cell bank: benefits to research, benefits to researchers, and quality control. A submission from 75 third-year Bachelor of Biomedical Science students at the University of Melbourne (Submission LRC449) said:

> We believe a human stem cell bank would be of great value to many areas of biology … including research into assisted reproduction, cancer research, and basic research in cellular and developmental biology. *Third-year Bachelor of Biomedical Science students, University of Melbourne (Submission LRC449)*

Numerous submissions argued that improved access to cell lines (via a national stem cell bank) would benefit Australian research. Stem Cell Sciences Ltd said:

> Such a bank could provide researchers in both commercial and academic spheres access to stem cell lines derived in Australia, as well as cell lines from other countries under reciprocal arrangements. It is only through easy access to a wide range of unencumbered, high quality stem cell lines that advances in the field will be accelerated. *Stem Cell Sciences Ltd (Submission LRC318)*

In its submission, the New South Wales Ministry for Science and Medical Research listed several potential benefits of a national stem cell bank:

> A registry of information on research and available stem cell lines. A repository, source and distribution point of stem cells and lines (which would assist in minimising duplication of effort). Well described and quality-assured stem cell lines. A source of training and expertise on techniques. *Ministry for Science and Health, New South Wales (Submission LRC1016)*

Other comments included one from Associate Professor Jeremy Thompson, Deputy Director, Research Centre for Reproductive Health, University of Adelaide (Confidential submission LRC266, quoted with permission of the author), who said that a national stem cell bank would create a level playing field across the country, which in his opinion was one of the guiding purposes behind the Act.

AusBiotech's submission listed a number of benefits of an Australian stem cell bank:

> Access to a variety of lines will be faster, easier and cheaper than going overseas; provide the potential to set and maintain standards (not only of lines but of institutions/researchers that apply to have access to lines); less potential for problems to occur with lines during transportation; ensuring that the standard of Australian lines meets internationally recognised standards; support Australia's reputation as a world leader in this research; and enable more cost-efficient research. *AusBiotech Ltd (Submission LRC450)*

The use of a national stem cell bank as a quality control mechanism for stem cell research was mentioned at the public hearings and in several submissions. At the Sydney consultation, Dr Kuldip Sidhu, Chief Hospital Scientist, Diabetes Transplant Unit, Prince of Wales Hospital, Sydney said that there are 225 stem cell lines around the world; however, international quality control is difficult, because researchers do not know the cell type, karyotype or quality of most cell lines. Until the quality of international stem cell lines can be guaranteed, he recommended that Australia have its own quality control system.

Arguments against a stem cell bank

There were several different arguments against the creation of a national stem cell bank in Australia. The Queensland Government (Submission LRC930) suggested that the potential advantages of a national stem cell bank need to be balanced against the cost of establishing, managing and overseeing the bank, and that a national audit of Australian stem cell research should be undertaken to ascertain whether a national stem cell bank is currently needed.

A written submission from the World Federation of Doctors Who Respect Human Life (Victorian Division) stated that there was a clinical need for stem cell registries and banks of other cells (eg bone marrow cells), but no need for a stem cell bank:

> Our researchers have more than enough [stem cell lines] … From a clinical point of view, they [stem cell banks] are not necessary. *World Federation of Doctors Who Respect Human Life (Victorian Division) (Submission LRC682)*

Some scientific researchers also argued that an Australian stem cell bank may not be necessary. At the public hearings, Professor John Rasko, Group Head, Gene and Stem Cell Therapy, Centenary Institute of Cancer Medicine and Cell Biology, and Royal Prince Alfred Hospital; Professor Alan Trounson, Director of the Monash Immunology and Stem Cell Laboratories at Monash University; and Reverend Dr Colin Honey, Chair, Stem Cell Ethics Australia, all indicated that it may be unnecessary for Australia to develop its own stem cell bank, as overseas stem cell banks (eg the United Kingdom cell bank) are adequate.

At the Melbourne public consultation, Reverend Dr Colin Honey, representing Stem Cell Ethics Australia, said that the:

> UK cell bank is good already. [I am] not sure if a national bank is necessary yet. Present provision [with the Australian Stem Cell Centre] is working and development of a bank in Australia may be a duplication. [Stem Cell Ethics Australia] remains unconvinced. *Reverend Dr Colin Honey, Chair, Stem Cell Ethics Australia (Melbourne hearings)*

He also said that:

> [It] doesn't really matter where the work is done — if there is a strong centre overseas then it doesn't matter if our researchers go there to do it. *Reverend Dr Colin Honey, Chair, Stem Cell Ethics Australia (Melbourne hearings)*

Some submissions were concerned about a national stem cell bank because of the scientific risks (eg tumour formation) of using stem cells. Mr Kenneth Glasgow, Northern Territory, said:

> If the research mentioned earlier which shows that embryonic stem cells mutate after a period of time (and a number of divisions) applies to [adult stem cells] as well it would not only be undesirable to have a National Stem Cell Bank, but dangerous. *Mr Kenneth Glasgow, Northern Territory (Submission LRC442)*

Many submissions were opposed to the establishment of a national stem cell bank for anything other than placental and adult stem cells. Mr Robert and Mrs June Mears submitted:

> We oppose the establishment of a National Stem Cell Bank for anything other than placental and adult stem cells. Adult stem cells are now providing successful therapeutic benefits; Australia should be putting its resources into this area of medical and scientific research. *Mr Robert and Mrs June Mears (Submission LRC653)*

Mrs Nola Drum, New South Wales, was concerned that the driving forces behind a national stem cell bank were profit and commercial outcomes:

> This bank is simply to create an industry which will be making millions for someone out of our future citizens. *Mrs Nola Drum, New South Wales (Submission LRC273)*

Administration of a national stem cell bank

Several submissions suggested models for the administration of a national stem cell bank. Some submissions said that the Australian Stem Cell Centre's Major National Research Facility, which is currently distributing MEL cell lines, would be well positioned as a basis for a future national stem cell bank. Researchers from Monash University said that:

> Both adult and embryonic stem cells are being banked at this facility which provides national access to banked cell lines for all Australian scientists and importantly, training to grow and differentiate these stem cells. *Dr Martin Pera and others, Monash University (Submission LRC509)*

Other submissions recommended that a national stem cell bank be based on the UK Stem Cell Bank (which requires a sample of any stem cell line generated to be deposited). Stem Cell Sciences Ltd said:

> The Australian stem cell bank should be a publicly funded organisation in line with the UK Stem Cell Bank. As occurs in the UK Stem Cell Bank, it could be a condition of NHMRC licensing of human embryo research that a sample of any stem cell line generated is deposited in the national stem cell bank. *Stem Cell Sciences Ltd (Submission LRC318)*

Some submissions recommended that the national stem cell bank either include, or be replaced by, a registry of stem cells available. This registry may be more cost-effective than a bank, and could also include verification that deposited cells were produced and maintained according to Australian standards.

Stem Cell Sciences Ltd said:

> The bank could maintain a registry of all stem cells available in Australia, which would include verification that deposited lines were derived in conditions consistent with Australian standards. This registry would be invaluable to institutional HRECs when assessing individual research applications, by preventing unnecessary lengthy and repetitious verification of the cell lines' origin and donor consent. *Stem Cell Sciences Ltd (Submission LRC318)*

At the Melbourne hearings, the Hon John Brumby, Victorian Treasurer and Minister for Innovation, recommended that a national stem cell bank would be best managed in national legislation with national and state agreements. At the same hearings, AusBiotech recommended that a bank be made independent by statute.

Other recommendations included establishing a virtual national stem cell bank:

> The national stem cell bank should be a virtual facility, ideally with no more than one bank in each city. This is a cost-effective way of achieving the desired outcome, and will facilitate the increased use of hESC because it is decentralised. *Diabetes Transplant Unit, Prince of Wales Hospital, Sydney (Submission LRC180)*

> An approach of interest expressed by some NSW researchers is the creation of a virtual bank or nodal approach. Consideration should also be given to adopting a staged approach. For example, the process could commence with the establishment of a registry, with other functions added over time. *Ministry for Science and Medical Research, New South Wales (Submission LRC1016)*

Sydney IVF (Submission LRC819) and Salt Shakers (Submission LRC624) suggested that a stem cell bank should be similar to existing blood and national cord blood banks.

Community involvement

Fair access and equal involvement were the two main concerns about community involvement in a national stem cell bank.

One submission recommended that material in a publicly funded stem cell bank should be publicly available, without prohibitive transfer fees or processes (Confidential submission LRC307). At the Sydney hearings, Professor Alan Trounson, Director of the Monash Immunology and Stem Cell Laboratories, Monash University, said that material transfer agreements attached to stem cell lines sometimes limit access or commercialisation, even if the lines are in a stem cell bank (such as the United Kingdom bank). Agreements between governments would therefore also necessary to guarantee that cells were accessible to everyone.

To ensure equal community involvement in a national stem cell bank, Dr Rachel Ankeny and colleagues called for explicit mechanisms to involve all sections of the community:

> … we encourage the LRC to recommend explicit mechanisms for active community involvement on an ongoing basis in setting research priorities and in decision making about how to select which lines to establish. This community involvement is especially important because banking might allow closer matching (and hence likely more effective therapies) for certain ethnic or minority groups (eg Aboriginal and Torres Strait Islander Australians) who might otherwise be disadvantaged if research and future therapies are reliant on the usual sources of donated embryos (given they are currently provided only by those who have undergone ART) or internationally-established lines (such as those in the UK). Attention to perspectives and views of such minority groups who are also typically vulnerable populations is essential for the ethical establishment of such a bank in the Australian context.
> *Dr Rachel Ankeny, Sydney University, Associate Professor Susan Dodds, University of Wollongong and Associate Professor Wendy Rogers, Flinders University (Submission LRC515)*

This submission also recommended that women be key community members to be consulted during the creation of a national stem cell bank.

At the Darwin consultation, Gareth Lewis, an acting Anthropology Manager of the Northern Land Council, said that Indigenous people may be concerned about the potential for exploitation if stem cells from minority groups were available for research in a stem cell bank.

The Christian Democratic Party, New South Wales, believed the community could be encouraged to donate to a national adult stem cell and cord blood stem cell bank:

> Community response could be elicited through the Red Cross Blood Bank or an entity adjunct to or associated with this bank. *Christian Democratic Party, New South Wales (Submission LRC820)*

Access by Australian researchers to stem cell banks in other countries

The Diabetes Transplant Unit, Sydney (Submission LRC180) stated that an Australian stem cell bank would interact with international stem cell banks. At the Sydney public consultation, Professor John Rasko, Group Head, Gene and Stem Cell Therapy, Centenary Institute of Cancer Medicine and Cell Biology, and Royal Prince Alfred Hospital, also referred to access to other stem cell banks:

> [The] UK Bank will be universally accessible under rigorous conditions. However, [we] do need good manufacturing practice conditions in this country so that technology can be transferred to the therapeutic situations when appropriate (monitored by TGA).
> *Professor John Rasko, Group Head, Gene and Stem Cell Therapy, Centenary Institute of Cancer Medicine and Cell Biology, and Royal Prince Alfred Hospital (Sydney hearings)*

Financial implications

Sydney IVF warned that a national stem cell bank would be expensive to maintain (Submission LRC819). The Diabetes Transplant Unit, Sydney (Submission LRC180) recommended that a national stem cell bank be federally funded, and that introducing cost recovery at the outset would slow the progress of research, especially in public institutions:

> The Diabetes Transplant Unit believes that the cost of supervising the making of hESC lines and any national stem cell bank agreed to should be paid for federally, at least for the next five years. Introducing cost recovery at present will significantly disadvantage progress in the field, especially where public institutions are involved. *Diabetes Transplant Unit, Prince of Wales Hospital, Sydney (Submission LRC180)*

Excess ART embryo bank or register

IVF Australia (Submission LRC346) recommended forming a national embryo bank in conjunction with a national stem cell bank for couples who wish to donate their excess embryos for stem cell research but who are not undergoing ART treatment at a clinic that has an active embryo research program.

15.4 Summary — stem cell banks

There are now a number of stem cell registries around the world holding information about the source, characteristics and derivation of stem cell lines. The International Stem Cell Forum (located in the United Kingdom) was also set up to bring together international research agencies into a formal mechanism for large-scale international collaboration.

There are also stem cell banks that are currently active or being planned in numerous countries around the world. These include the United Kingdom, the United States, Sweden, China, South Korea and the United Arab Emirates. The United Kingdom Stem Cell Bank, funded by the United Kingdom's Medical Research Council and Biotechnology and Biological Sciences Research Council, began

operating officially in January 2003 and will ‘curate ethically sourced, quality controlled adult, fetal and embryonic stem cell lines and will be open to academics and industrialists from the United Kingdom and overseas’.

Support for an Australian national stem cell bank was given in many written and oral submissions. Written and oral submissions identified the main advantages of a national Australian stem cell bank as being:

- improved access to stem cell lines for research
- using the bank as a quality control mechanism for stem cell research.

However, some submissions gave only conditional support for a stem cell bank, provided the bank excluded embryonic stem cells. Others suggested that a cord blood bank be set up.

There were several different arguments against the creation of a national stem cell bank. Some scientific researchers believe that an Australian stem cell bank may not be necessary because overseas stem cell banks (eg the United Kingdom cell bank) were adequate. Others worried that the driving forces behind a national stem cell bank were profit and commercial outcomes.

Different models for the administration of a national stem cell bank were suggested. Some recommended that a national stem cell bank be established at the Major National Research Facility at the Australian Stem Cell Centre, which is already capable of storing stem cell lines. Other suggestions were that a national stem cell bank be based on the UK Stem Cell Bank, that a registry of stem cells available would be a better system or that an Australian stem cell bank be a decentralised structure incorporating ‘nodes’ of specific research interest or expertise located in the major capital cities.

Fair access and equal involvement were the two main concerns about community involvement in a national stem cell bank. There were also concerns raised about the potential for exploitation of stem cells from minority groups.

Regarding funding of a stem cell bank, some commented that the bank would be expensive to maintain, while others recommended that a national stem cell bank be federally funded.

Finally, it was also proposed that a national excess ART embryo bank/register be established in conjunction with a national stem cell bank to allow more couples to donate their excess embryos for research if they wish to do so.

16 Approaches to legislation

In the course of the reviews, the Committee considered how the current legislative approach deals with the complex and changing biotechnology involved. This chapter presents the Committee's analysis in terms of the current arrangements and other regulatory models, and the comments received in the submissions and hearings relating to this issue.

16.1 Prescriptive versus regulatory models of legislation

Prescriptive legislation

The Committee identified three areas of concern about the development and application of prescriptive legislation in this area:

- difficulties associated with drafting legislation in areas of rapid technological and scientific advance
- difficulties in the interpretation of legislation
- lack of legal protection for researchers.

Drafting legislation in areas of rapid technological and scientific advance

If activities are not contemplated when legislation is being drafted, or the scientific basis of those activities is not fully understood, they may be 'accidentally' prohibited when, if considered in the light of new knowledge, that might not be the intention. For example, the PHC Act s20(2) states that it is an offence to create a 'hybrid embryo'. Section 8(1) defines a 'hybrid embryo' as '(b) an embryo created by the fertilisation of an animal egg by human sperm'. The aim of this provision was presumably to assuage community concern that new technologies might be used to make half-human, half-animal hybrids of the type depicted in science fiction. But this prohibition has also had the effect of prohibiting a clinical test for the viability of human sperm that is routinely undertaken in other countries. Instead of testing the sperm by attempting to fertilise a human egg, the sperm is tested on a hamster egg (which is then immediately discarded). The hamster test avoids the need to use human oocytes to test sperm for viability, which is important in clinical assisted reproductive technology (ART) practice (see Section 4.3). As discussed in Section 4.3, the current provisions of the Acts have also prevented work to develop safer and improved methods of egg collection, development and storage for use in ART treatment.

Conversely, activities that are intended to be prohibited may be 'accidentally' allowed. For example, the PHC Act prohibits various types of research on embryos, and an 'embryo' is defined as 'a *live* embryo' (s8(1), emphasis added). One might question whether people would agree that embryos that have been left to 'succumb' should then be available for unregulated research on the basis that they are no longer 'live'. Certainly, many people believe that such embryos, if left to succumb, should be disposed of respectfully and not used for other purposes without ethical approval and proper consent. Yet this is not the effect of the legislation.

Difficulties in the interpretation of legislation

Another problem is that it may also be difficult, when interpreting legislation, to know whether or not an activity is covered by the legislation. For example, the RIHE Act s20(1) states that a person may apply to the Licensing Committee for a licence authorising the use of excess ART embryos. The term 'excess ART embryo' is defined in s9(1), but this requires reference not only to the procedure by which the embryo is declared 'excess', but also to the meaning of an 'embryo'. Although, as noted above, an embryo must be 'live' to fall within the definition in the Act, the definition does not require that it must

be ‘viable’. Thus, a ‘human embryo’ might include entities that have no potential for human development, including those with gross chromosomal defects such as aneuploidies. Therefore, it is not clear whether researchers can lawfully do research on such entities without a licence, or whether the Licensing Committee can grant a licence to undertake such research.

Lack of protection for researchers

Furthermore, if legislation is unclear or ambiguous, it is possible that scientists may undertake research that is prohibited, believing it is lawful, and then face a potential fine and prison sentence. Similarly, a researcher may face criminal prosecution if they do research that requires a licence, but they do not obtain a licence because they do not believe it is necessary. Although a prosecution is unlikely in such circumstances, especially in the absence of criminal intent (*mens rea*), there is still the possibility of a prosecution and even a conviction if the law is strictly applied.

This is a breach of the basic legal principle of the rule of law, which states that all statutes, especially those that carry a prison sentence, should be promulgated in advance and should be capable of being understood. Unclear provisions are also a disincentive for scientists to undertake research and for industry to fund it. Scientists will be reluctant to do projects when they are not sure whether the projects are lawful. This is especially the case when research projects involve considerable expenditure. Sponsors, whether public or private, will naturally want to be assured that they will be able to benefit from commercial applications of the research results, which may not occur if there is doubt about the legality of the research.

Moreover, if legislation is unclear or ambiguous, it is no answer to say that scientists can obtain a licence, whether they need one or not, if they are in doubt about the applicability of the legislation to their proposed project. The Licensing Committee will have the same difficulties as other people in interpreting the legislative provisions and, as the legislation stands at present, the Licensing Committee has no discretion in applying and interpreting it. The Licensing Committee cannot override the statutory provisions. If it grants a licence for research that is later ruled by a court to contravene the Act, it will be no defence to the researcher that he or she obtained a licence.

Concerns expressed during the consultation process

Concerns about the prescriptive nature of the legislation were expressed in many submissions to the reviews (see Section 16.2), and many respondents emphasised the need for greater flexibility in the regulatory system. The Licensing Committee in particular mentioned difficulties that it had experienced because of the nature of the current legislation. At present, the Committee has no leeway to grant a licence that is not clearly permitted by the Act, even if the purpose of the proposed research is closely related to activities that are permitted by the Act. Also, the Committee has no legislative power to provide advice to applicants for licences. Any advice that is provided informally would not protect researchers from legal repercussions if their project is later found by a court to have been in breach of the legislation.

A more flexible approach: regulations, guidelines and rulings

A more flexible approach than that ordinarily provided by legislation can be achieved by the use of regulations, guidelines and rulings from a regulatory agency.

The PHC Act and the RIHE Act already empower the Governor-General to make regulations. These are more flexible than legislation, because they can be made without passing through the full parliamentary process, while being subjected to parliamentary scrutiny by being tabled in parliament for consideration for the required period. However, there is necessarily a delay in the drafting and publication of regulations, especially because the two Acts require the States to be consulted before any regulations are made. Also, regulations can be made only on matters ‘*required or permitted by*

[the] Act' or 'necessary or convenient to be prescribed *for carrying out or giving effect to this Act'* (PHC Act s26; RIHE Act s48; emphasis added). The regulation-making powers are therefore limited and may sometimes be unclear.

Publication of guidelines by a regulatory agency is another means of increasing the flexibility and responsiveness of a regulatory scheme. Guidelines can be readily altered in the light of new research and knowledge. Also, a regulatory agency can be empowered to take account of such guidelines, even though they are outside the Act. Under the RIHE Act s21(4)(c), the Licensing Committee already has the power to take account of external guidelines in granting licences. However, the Licensing Committee cannot grant licences for research that falls outside the literal provision of the Act, even if the projects seem close to those intended to be covered by the Act. The committee also cannot provide advice to applicants for licences, or anyone else, in a way that provides any statutory protection to those who act in good faith on the basis of that advice.

A third method of giving the Licensing Committee the full flexibility it needs in a rapidly developing area, such as genetic research and other aspects of biotechnology, is to enable it to give 'rulings' about the interpretation of the legislation. These rulings could be backed by a legislative provision that researchers who act on the basis of such rulings are protected from potential prosecution. This approach has precedents in other areas of regulatory activity, such as the *Trade Practices Act 1974*, which formerly enabled the federal Trade Practices Commissioner to give rulings on the interpretation of the Act. Similarly, the Commissioner of Taxation gives rulings from time to time on the applicability and interpretation of various Acts dealing with income tax.

Empowering the Licensing Committee to give rulings about the interpretation of the PHC Act and the RIHE Act, and to report on those rulings at once to the NHMRC and Parliament, could be done by relatively minor changes to the existing legislation. Section 41 of the RIHE Act already appears to give the Licensing Committee powers under both Acts, and the RIHE Act already imposes rigorous reporting requirements on the Licensing Committee. Under that Act, the Licensing Committee is required to provide information to the NHMRC; it must report directly to parliament on fixed dates and it may also report to parliament at other times; and it must notify applicants, human research ethics committees and relevant State bodies of its decisions concerning applications for licences. This provides a comprehensive system for ensuring transparency in the granting of licences. If the Licensing Committee were empowered to give rulings when granting licences, it would thus be in accordance with the existing legislation to extend the reporting requirement to apply also to its rulings.

Similar arguments could be advanced to empower the Licensing Committee to give rulings under the PHC Act on the legality of proposed activities. If the Committee were empowered to give rulings on whether particular conduct would be in breach of the Act, and required to report the ruling immediately to the NHMRC and to parliament, researchers could be advised promptly whether proposed research would or would not fall within the Act and parliament would be informed. This procedure would have the additional advantage of assuaging community concern about the possibility that research that is not currently anticipated may be undertaken because it is believed to fall outside the Act when that may not be the case.

Under these arrangements regarding rulings, any ruling given by the Licensing Committee that enables a licence to be granted where it may fall outside the current purview of the legislation could be quickly identified and an appropriate response made. For example, as suggested above, if there is serious concern about whether it was appropriate to grant a licence in a particular case, the licence could be revoked or varied after the Licensing Committee's report is tabled in parliament. This is in line with the committee's powers under the existing legislation to grant and vary licences.

In relation to rulings given under the PHC Act, if parliament is concerned about the interpretation that the Licensing Committee has given concerning any provision of the legislation, an immediate response could also be made by means of a Regulation made by the Governor in Council. Both the PHC Act and the RIHE Act have broad regulation-making powers, although as noted above, the requirement to consult the States before making new regulations makes this more complex than for other regulations.

Therefore, if the current legislation were amended to grant the Licensing Committee some discretion under the two Acts to give rulings when granting licences or interpreting the provisions regarding conduct covered by the PHC Act, the requirement to report to parliament at once on the Licensing Committee's ruling would provide more flexibility than the present system, while still ensuring that the Licensing Committee and researchers remain accountable through a transparent decision-making process.

Such an approach would also complement the current model for monitoring compliance with the two Acts, which has been developed based on the legal theory of the 'regulatory triangle'. That is, that those who are regulated (in this case the scientists) are presumed not to be intending to break the law deliberately and that they should be assisted in their efforts to comply with it; prosecution should be the final resort (see Chapter 10). Such a regulatory approach may reduce the need for further reviews of the legislation outside the usual parliamentary process of amendment.

16.2 Submissions and hearings

Structure and titles of the Acts

The Committee received several comments and submissions relating to the structure of the legislation, and specifically to whether there should be two Acts (as is currently the case) or whether the RIHE Act and PHC Act should be combined into a single Act. Opinions on this issue were generally not very strong in either direction. However, Professor Agnes Bankier, representing Genetic Health Services Victoria, expressed the view at the Melbourne hearings that human cloning for reproductive purposes should be clearly distinguished and separated in the legislation from cloning using somatic cell nuclear transfer. She also advised against the use of the term 'cloning':

> In fact the very word 'cloning' has become so laden with emotion that it can cloud our thinking and is best avoided. *Professor Agnes Bankier, representing Genetic Health Services Victoria (Melbourne hearings)*

Mr Adam Johnston, New South Wales (Submission LRC287) also suggested that the terms 'human cloning' and 'human embryos' in the titles of the Acts were too emotive and that more appropriate titles for the Acts might be 'Research Involving Certain Tissues Obtained from Individuals' Act (for the RIHE Act) and 'Prohibition of Certain Specified Actions Involving Somatic Cell Nuclear Transfer' Act (for the PHC Act).

Flexibility in the regulatory system

In its meeting with the Licensing Committee in Adelaide, the Legislation Review Committee heard that flexibility in the regulatory system is essential to allow for rapid and unforeseeable advances in technologies associated with human embryo research. Many submissions, especially from researchers and governments, also raised this issue. For example, the submission from the Victorian Government stated:

> The field is developing rapidly and the legislative framework needs to be flexible to keep pace with technological developments and the requirements of the researchers in order to enable ethical research that will benefit the community. *Victorian Government (Submission LRC537)*

The importance of ensuring that the legislation keeps pace with scientific advances led many respondents, including several State governments, to the view that the legislation should be reviewed regularly:

> In addition to those specific responses, the Department also recommends … a further review in 3 to 5 years. Legislation regulating any area of rapidly evolving biotechnology should be reviewed regularly to ensure that it continues to address emerging challenges and to apply appropriate ethical oversight. *South Australian Department of Health (Submission LRC576)*

> In light of the rapid advances in technology, WA considers that the legislation should be subject to ongoing review. *Government of Western Australia (Submission LRC782)*

> Supported: provision for future monitoring and review of the legislation and regulatory framework given rapid developments in this field. *Ministry for Science and Medical Research, New South Wales (Submission LRC1016)*

> I'd support an ongoing process of review. I think obviously you'd want to do your best at getting the definitions right now and having an open enough mind to be careful that those definitions are broad and all encompassing. But the pace at which this field is changing is quite phenomenal and I think it would be very sensible to have a review time for it. *Associate Professor Melissa Little, Institute for Molecular Bioscience, University of Queensland (Brisbane hearings)*

> The problem has always been the flexibility of scientists and the incredible agility of science … And when things are moving so fast it's very hard to legislate and make decisions that are going to be lasting and very thoughtful. I see an absolute obligation … to have an ongoing review process. And although I entirely appreciate that legislation is fixed in stone for the period that it's legislated for, it is important to have some form of sunset clause and it is important to have a review integrated into the Act I believe so that we can review the developments in science that have occurred since the previous review. *Professor John Rasko, Group Head, Gene and Stem Cell Therapy, Centenary Institute of Cancer Medicine and Cell Biology, Royal Prince Alfred Hospital (Sydney hearings)*

> These types of changes and the speed of change highlight the need to ensure that legislation is progressive, flexible and able to respond to this dynamic field. AusBiotech is strongly of the view that at the very least, both the *Prohibition of Cloning Act 2002* and the *Research Involving Human Embryos Act 2002* require review at least every three years to ensure their on-going relevance. *AusBiotech Ltd (Submission LRC450)*

> The Acts should remain under review from time to time to enable new directions and benefits to be pursued for treatment of otherwise intractable pathologies and injuries. It is not always possible to predict the outcomes and direction of research and important new developments which could be severely hampered unintentionally by legislation. *Dr Martin Pera and others, Monash University (Submission LRC509)*

Because amendment of legislation to take into account scientific advances is a time-consuming and cumbersome process, some respondents expressed a preference for some type of legislative framework that allows greater flexibility and responsiveness than an Act of Parliament:

> My general view would be I think, when you're legislating in an area in this particular science where the knowledge is accelerating and changing and being transformed so rapidly, it would seem to me the intelligent thing for the legislator to do would be to set a framework of law which provided in-principle support … but we'd set up either an advisory or a regulatory framework which had within it the flexibility to apply those principles according to the context [of] the emerging science. *Dr Paul Brock, representing the Coalition for the Advancement of Medical Research Australia (Sydney hearings)*

> Legislation is likely to be a cumbersome mechanism that doesn't respond sufficiently to the science … But the model we've seen in Britain where public consultation is part of the process, where only those matters that are of fairly clear mind are legislated against, and there is provision for the Committee to operate a little like the regulation of reproductive technology that has been done so successfully in Australia. *Reverend Dr Colin Honey, Chair, Stem Cell Ethics Australia (Melbourne hearings)*

During meetings in Adelaide, the Licensing Committee also told the Legislation Review Committee that the highly prescriptive nature of the legislation presents problems for the work of the Licensing Committee, and that it would be preferable to have a framework that would allow both periodic updating of the Acts and greater flexibility for the Licensing Committee in applying the legislation.

16.3 Summary — approaches to legislation

While it is generally accepted that there is an ongoing need for legislation in this area, it was also widely acknowledged that prescriptive legislation has a number of disadvantages, because it is difficult to anticipate advances in knowledge and potential new uses of the technologies. This difficulty, combined with the complexity of the science involved, inevitably leads to ambiguities and difficulties in interpretation. In the absence of a binding 'ruling' from a regulatory agency (similar to the rulings issued by the Commissioner of Taxation), such ambiguity can leave researchers unfairly exposed to prosecution.

Regulations and guidelines are more flexible than legislation but cannot provide the immediate response that may be needed in some cases. If the Licensing Committee were given power to make binding rulings on its interpretation of the legislation, that would provide the necessary flexibility in its application. As in the present legislation, these rulings could be subjected to parliamentary scrutiny by a legislative requirement that the Licensing Committee must report immediately on its rulings to the NHMRC and to parliament and that the rulings must be tabled in parliament for its consideration. Thus, in the cases of both the PHC Act and the RIHE Act, a combination of legislation, regulations, guidelines and Licensing Committee rulings, together with rigorous parliamentary and community reporting, could provide an accountable and flexible system in line with the expectations of the government, researchers and the community. This may also avoid the need for further reviews of the legislation outside the usual parliamentary process of amendment.

Part C
The Committee's view and recommendations

17 The Committee's view and recommendations

17.1 Introduction

Throughout the consultation, the Committee heard from a broad range of people about the implications of legislation for assisted reproductive technology (ART), including in vitro fertilisation (IVF), and for human embryo research. The purpose of this public consultation was to seek the views, values and 'standards' of the community regarding the reviews of the *Prohibition of Human Cloning Act 2002* (PHC Act) and the *Research Involving Human Embryos Act 2002* (RIHE Act). In doing so, the Committee came to the view that Australian society should not be characterised as being a single, homogeneous community, but instead is composed of many different 'communities', each of which may have its own perspectives, interests and values, and that any one individual may be a member of many different communities at the same time. Thus, a person may be a committed Christian, a scientist, a shareholder, and the relative of a person with a serious illness — 'communities' that may have very different perspectives or 'standards' regarding the development and use of embryos for research.

The Committee also observed that the 'standards' evidenced by these communities varied enormously both between and within communities in terms of the extent to which they were clearly developed or articulated; the degree to which they were felt to bind members of the community; and the degree to which they changed over time or with developments in science and medicine. Consequently, the Committee considers that the social and moral concerns raised by ART and embryo research cannot be explained simply by reference to a single 'standard' or a single set of values, beliefs or interests held by a single community.

In looking for common ground, the Committee noted that there are certain moral values that are held in common by all communities, such as a commitment to social justice and equity, and to the care of vulnerable members of society. This is reflected in broad support for medical research aimed at understanding, preventing or treating disease. The Committee also noted widespread support for medical research to assist people to have children (including a general acceptance that this process may involve the 'wastage' of some embryos). Hence, the Committee came to the view that considerations regarding the use of embryos for research needed to take account of both the value that different communities attach to the embryo, and the social and moral value that communities attach to the treatment of disease and the amelioration of infertility.

It is clear that there are wide-ranging views on embryo research and human cloning, with the exception of human reproductive cloning, which appears to be widely condemned. Some people consider that human embryos have the moral status of an adult and so should not be subject to destructive research in any circumstances, regardless of medical benefit. Others hold a view that human embryos deserve some special consideration by virtue of their moral or social/relational status, but should not be accorded the same status as humans after birth. People who hold this view consider that embryos may be subject to research in certain circumstances, such as when they are judged to be excess, nonviable or unsuitable for implantation. A third group supported research on human embryos before implantation into the body of a woman and urged an extension of what is currently permitted because of the potential medical or scientific benefits that may result from such research. Each of these views is sincerely held and it was apparent to the Committee that all those who made submissions were motivated by a desire to do what is best for our society. However, it was also clear to the Committee that these views could not always be reconciled. Therefore, the challenge for the Committee has been to make recommendations that are consistent with shared values and take into account the needs, beliefs and concerns of the whole community.

In framing the recommendations, the Committee considered that the higher 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 there is evident or possible harm, or where there is widespread and deeply held community objection, a total prohibition through the legal system may be justified. The Committee's view is that it does not necessarily follow that even though some people think that an activity is unethical, it is necessary to make that activity illegal. Furthermore, the wider the range of ethical views on a particular activity, the weaker the case becomes for declaring that activity to be illegal, with all the attendant consequences of criminal conduct.

17.2 National legislation

In 2002, the Australian Parliament and the Council of Australian Governments (COAG) agreed to prohibit human cloning in any form, to prohibit some other assisted reproductive technologies, and to restrict research involving human embryos to those that were excess to ART clinical programs. On the other hand, the Australian Parliament and COAG allowed research using excess ART embryos for clinical improvements and training in ART, and for scientific research to develop human embryonic stem cells.

In the case of human cloning and the other reproductive technologies covered by the PHC Act, the reasons for the prohibitions included ethical concerns about social and psychosocial effects of using the technologies to produce live human beings, and medical and scientific concerns about the safety of such procedures. In the case of research involving human embryos, the reasons underpinning the RIHE Act were community concerns about the creation of human embryos by any other means apart from fertilisation of a human egg by a human sperm, and their use for any purpose apart from seeking to achieve a pregnancy in a woman.

The Committee established that some of these concerns remain today. Because of the divergent values and interests represented within Australian society, some disagreement is likely to remain if no changes are recommended to the legislation, or following the passage of any amended national legislation regulating embryo research and human cloning.

One approach would be to make participation in human embryo research a matter of individual conscience, and to avoid legislation about these matters. However, on the whole, both proponents and opponents agree that the current system of legislation is valuable. The opponents of embryo research agree that regulation and supervision of such research is preferable to no restrictions. The proponents concede that the present system provides a means whereby their research is supervised and given approval to proceed. Most respondents to the reviews also supported the continuation of legislation to maintain the prohibition of human reproductive cloning and other reproductive practices considered unacceptable or unsafe.

The Committee concludes that Australia should continue to have national legislation imposing prohibitions on reproductive cloning and some other ART practices, as well as strict control and monitoring, under licence, of human embryo research.

Recommendation — national legislation

1. Clinical practice and scientific research involving assisted reproductive technologies (ART) and the creation and use of human embryos for research purposes should continue to be subject to specific national legislation.

17.3 Prohibited practices

The Committee considers that most of the practices that are currently prohibited in the Acts should continue to be prohibited. This includes a total prohibition on reproductive cloning.

The Committee also considers that there should continue to be a total prohibition on the implantation, into the body of a woman, of embryos other than those created by the fertilisation of a human egg by a human sperm.

Furthermore, the Committee also holds the view that the creation of embryos other than by the fertilisation of a human egg by a human sperm should also continue to be prohibited except for the limited circumstances indicated below and in Section 17.4, where the Committee suggests that some such embryos could be created and used for research purposes but never implanted into the body of woman.

These prohibited practices are discussed in detail in the remainder of this section. Prohibitions on import, export and commercial trading of embryos and gametes are discussed in Sections 17.11 and 17.12.

Reproductive cloning

The Committee heard strong agreement between all groups that human reproductive cloning should continue to be prohibited on ethical grounds. The serious health and safety issues associated with the birth of live, cloned animals was also seen as a reason to prohibit this procedure in humans. The Committee's view is that the prohibition of human reproductive cloning should be maintained because of these ethical and safety concerns.

Recommendation — reproductive cloning

2. Reproductive cloning should continue to be prohibited.

Developing and implanting embryos categorised as 'prohibited embryos'

The Committee considered the 'prohibited embryos' mentioned in the PHC Act. These include:

- embryos created by nuclear transfer
- embryos created by other methods not involving fertilisation of eggs by sperm
- human–animal hybrid or chimeric embryos
- embryos with genetic material from more than two people
- embryos with genetic alterations.

The Committee noted that there was strong community objection to the implantation of such prohibited embryos into the body of a woman or to their development in any other way beyond 14 days. The Committee sees no reason to depart from this strong community objection.

The Committee's view on the creation of embryos by nuclear transfer or other methods not involving fertilisation of eggs by sperm is discussed in Section 17.4.

The Committee noted that the creation of human–animal hybrid or chimeric embryos[44] was only mentioned in a few of the submissions and hearings. However, there was an implicit understanding that the creation of such entities could be of concern to the community. Therefore, the Committee's view is that creation of such embryos for reproductive purposes (that is, development beyond 14 days and implantation of such embryos) should continue to be prohibited.

However, because of the potential benefits, and to avoid the need for obtaining additional human gametes for research purposes, the Committee considers that fertilisation of animal gametes by human gametes should be permitted up to, but not including, the first cell division, to allow testing of human gamete maturity or viability as indicated in Recommendation 17.

The Committee also suggests that, under limited circumstances, human–animal hybrid or chimeric embryos could be used, under licence, for preliminary investigations of nuclear transfer technologies. The Committee reached this view because this procedure could reduce the need for human egg donation (see Recommendation 24).

Similarly, with respect to embryos with more than two genetic parents (including those created using cytoplasmic transfer), embryos using precursor cells from a human embryo or a human fetus, and embryos carrying heritable changes to the genome, the Committee's view is that the creation of such embryos for reproductive purposes should remain prohibited (that is, development and implantation of such embryos should be prohibited) due to the lack of social support for these practices and concerns about safety.

However, the Committee's view is that these methods could be used for research, under licence, to advance knowledge and investigate specific diseases and conditions. Further discussion of these proposed licensed activities is included in Section 17.4.

The Committee also considers that placing any human embryo into an animal or into the body of a human apart from into a woman's reproductive tract, or placing an animal embryo into the body of a human for any period of gestation, should also continue to be prohibited because these practices are repugnant to the community. Similarly, the Committee did not hear any arguments for lifting the prohibition on the collection of viable embryos from a woman and therefore considers that this prohibition should continue.

44. Embryos created by fertilisation or activation of any combinations of human and animal gametes or cells, or embryos into which an animal cell or part of an animal cell has been introduced (see Glossary)

Recommendations — prohibitions on developing and implanting embryos

3. Implantation into the reproductive tract of a woman of a human embryo created by any means other than fertilisation of an egg by a sperm should continue to be prohibited.
4. Development of a human embryo created by any means beyond 14 days gestation in any external culture or device should continue to be prohibited.
5. Implantation into the reproductive tract of a woman of a human–animal hybrid or chimeric embryo should continue be prohibited.
6. Development of a human–animal hybrid or chimeric embryo should continue to be prohibited, except as indicated in Recommendation 17.
7. Placing a human embryo into an animal or into the body of a human apart from into a woman's reproductive tract, or placing an animal embryo into the body of a human, for any period of gestation, should all remain prohibited.
8. Implantation into the reproductive tract of a woman of an embryo created with genetic material provided by more than two people should continue to be prohibited.
9. Implantation into the reproductive tract of a woman of an embryo created using precursor cells from a human embryo or a human fetus should continue to prohibited.
10. Implantation into the reproductive tract of a woman of an embryo carrying heritable alterations to the genome should continue to prohibited.
11. Collection of a viable human embryo from the body of a woman should continue to be prohibited.

Creating human embryos for any purpose other than to achieve a pregnancy in a woman

During the review hearings, at the discussion forums and through the written submissions, the Committee heard a range of views on the status and potential of a human embryo (see Chapter 8). These views were underpinned by different values and beliefs about the time that human life starts, and the social and moral status of a human embryo. These beliefs, in turn, affected the relative weight placed on the right to life of a human embryo, the potential to help people have children, and the potential to improve or save the lives of people living with incurable diseases or injuries.

Currently, the prohibition of creating a human embryo for any purpose apart from to achieve a pregnancy in a woman prevents the creation and use of fresh embryos for research. The provisions of the RIHE Act for declaring embryos to be excess ART embryos and giving proper consent for research, have also precluded the immediate (fresh) use of any unfit or 'surplus' ART embryos (see Chapter 4).

The Committee therefore discussed the possibility of permitting the creation of embryos for research, particularly because some ART researchers also suggested that relaxation of current laws to allow the production of fertilised human embryos to be used for embryology studies would be beneficial to the further development of safe and successful ART treatments.

In this regard, the Committee noted that, in nature, many embryos fail to implant or to become a viable pregnancy. The Committee also noted that ART embryos that are surplus to reproductive needs are allowed to die. These arguments were used by some to justify the possible creation of embryos for research.

On the other hand, the Committee noted that a human embryo created by gamete fusion is regarded as a significant entity associated with the purpose of having babies.The creation of such embryos is widely accepted for helping people who would otherwise have difficulty having a family, but there is little general support for the creation of such embryos for research purposes. The Committee therefore

formed the view that the prohibition on creating human embryos by fertilisation (using human eggs and sperm) for any purpose apart from seeking to achieve a pregnancy should be maintained. However, as noted below, the Committee considers that research on eggs fertilised by sperm should be permitted up until the first cell division.

Recommendations — creation of human embryos by fertilisation

12. Creation of human embryos by fertilisation of human eggs by human sperm should remain restricted to ART treatment for the purposes of reproduction.
13. Creation of human embryos by fertilisation of human eggs by human sperm to create embryos for the purposes of research should continue to be prohibited except in the situation described in Recommendation 15.

17.4 Research and other activities involving human embryos permitted under licence

Use of excess ART embryos

Although some respondents to the reviews thought that all uses of human embryos should be prohibited, the Committee considered that, overall, there was support for the use of excess ART embryos in research under the provisions of the RIHE Act. This view was also heard from ART consumers, many of whom have donated their excess embryos for research.

Excess ART embryos have been used for research and other activities to improve the clinical practice of ART (see below) or for the derivation of embryonic stem cells. Many respondents expressed a view that embryonic stem cells are not required because adult stem cells could be used instead. In terms of this argument, the Committee carefully considered all the submissions on embryonic stem cell research and equivalent research on adult stem cells, and noted the following issues:

- Many of the arguments regarding the clinical utility of embryonic stem and adult stem cell research were based on speculation rather than on established data.
- While the findings of embryonic stem cell research have not yet translated into any clinical trials or treatments, the use of excess ART embryos to derive embryonic stem cell lines has contributed to progress in advancing our understanding of stem cells and research directed to future therapeutic outcomes of stem cell research.
- Although there has been substantial progress in adult stem cell research in the past few years, the developments in adult stem cell research do not remove the need to make progress in embryonic stem cell research. The Committee agrees with the views of the many researchers who consider that both types of research should continue.
- The range of diseases and conditions that may be treated by therapies developed from stem cell research is substantial, and therefore the number of people who may ultimately benefit from such research is high.

Therefore, the Committee's view is that further research on embryonic stem cells is required and that this provides a justification for the use of excess ART embryos for research purposes.

Some respondents suggested that ART clinics produce more ART embryos than required for treatment in order to ensure a supply of excess ART embryos for research. However, the Committee received no evidence that this is the case and therefore rejects this view. Furthermore, ART clinics told the Committee that the number of excess ART embryos that have been donated for research exceeds the number that is required for current research projects .

Information about the number of embryos created, implanted and stored is already provided by each ART clinic in its annual Reproductive Technology Accreditation Committee (RTAC) report (see Chapter 12). In practice, the number of embryos created and implanted per cycle of ART treatment has been decreasing over the past decade as techniques have improved and reduced the risks of multiple births (see Section 4.2).

The Committee also noted that the sunset clause (RIHE Act s46), which has now lapsed, was a response to similar concerns in 2002, and an instrument of government to provide time for the development of an appropriate licensing and inspection system. The licensing system is now in place and the RTAC monitoring and annual reporting mechanisms for ART clinics are well established. Therefore, the Committee concludes that there is no further need to restrict the use of excess ART embryos to those produced before a specified date or for any further mechanism for monitoring of this process.

Recommendation — use of excess ART embryos in research

14. Use of excess ART embryos in research should continue to be permitted, under licence, as under current legislation.

ART clinical practice and ART research

The Committee was concerned to hear that the legislation has had the apparently unintended consequence of preventing research into improved methods for achieving pregnancy in ART clinics. In particular, the legislation has stopped research on culture and maturation of immature eggs ('in vitro maturation of oocytes', or IVM), frozen oocyte storage, various aspects of in vitro fertilisation (IVF), and gamete (egg and sperm) development. The ability to produce mature oocytes in culture provides a way of reducing the use of follicle stimulating hormone and would therefore benefit women undergoing ART. It may also allow the production of mature oocytes from frozen ovarian tissue, such as tissue stored before cancer therapy.

The Committee heard that research on the maturation of eggs has been prevented under the current legislation, because testing the viability of mature eggs requires either fertilisation by sperm, or chemical activation (parthenogenesis). Under the definitions and prohibitions in the current legislation, both these activities are illegal. The development of methods to freeze oocytes and of better methods of fertilisation has also been prevented for similar reasons. In addition, the prohibition on creation of hybrid embryos, combined with the current definition of an embryo, has further limited IVF research (for example, by preventing tests of sperm quality involving fertilisation of hamster eggs).

The Committee considered several options for changes to the legislation to allow these areas of ART research to resume:

- changing the definition of a human embryo to a slightly later stage in the fertilisation process, in accordance with Victorian and other legislation that was in place before the national legislation was passed in 2002;
- removing parthenogenetic embryos from the definition of a human embryo or human embryo clone, thus allowing oocyte activation; or
- lifting the prohibition on creating embryos by fertilisation of eggs with sperm for research use.

The Committee noted that changing the definition of a human embryo to a slightly later stage in the fertilisation process (the first cell division) would allow much of the research described above to occur without breaking the law, while still maintaining a very broad definition of an embryo in line with all the community views expressed to them during the reviews. This is discussed in detail in Section 17.5.

In connection with the second option, the Committee heard from ART researchers and practitioners that, although parthenogenetic activation can be induced using chemical or other activation methods, it also occurs spontaneously in vitro and in nature. The Committee's view is therefore that intentional parthenogenetic activation of oocytes should be permitted, under licence, for development for up to 14 days, but that implantation of parthenogenetically activated oocytes into a women's reproductive tract should continue to be prohibited (see Recommendation 3).

The third option (permitting creation of embryos by fertilisation for research) is discussed in Section 17.3) and was rejected by the Committee.

The Committee also heard that requiring a licence for training and quality assurance activities has presented an administrative barrier to these necessary aspects of ART clinical practice activities. The current process of applying for a licence is time-consuming and not well suited to these activities, which depend on factors such as staffing requirements. Furthermore, at times, there may be a need for rapid action to resolve a specific quality assurance issue. However, in view of the strong community attitudes supporting the regulation of this sensitive area, the Committee's view is that all research involving human embryos should continue to require a licence. However, it is also the Committee's view that the licensing process for these activities could be facilitated by the Licensing Committee developing a proforma application for training and quality assurance activities in ART clinics.

Finally, it is the Committee's view that cytoplasmic transfer offers potential for the treatment of mitochondrial disease and to improve fertilisation for some women. Therefore, consideration should be given to research, under licence, on this procedure.

Recommendations — ART clinical practice and ART research

15. Research involving fertilisation of human eggs by human sperm up to, but not including, the first cell division should be permitted for research, training and improvements in clinical practice of ART.
16. Testing of human oocytes for maturity by fertilisation up to, but not including, the first cell division or by parthenogenetic activation should be permitted for research, training and improvements in clinical practice of ART.
17. Certain interspecies fertilisation and development up to, but not including, the first cell division should be permitted for testing gamete viability to assist ART training and practice.
18. The Licensing Committee should develop a simple proforma application for licences to undertake training and quality assurance activities for ART clinics.
19. Consideration should be given to the use of cytoplasmic transfer (including transfer of mitochondrial DNA), under licence, for research on mitochondrial disease and other uses to improve ART treatment.

Use of fresh embryos, including pre-implantation genetic diagnosis embryos

The Committee heard several arguments in favour of using fresh embryos (rather than frozen embryos) for ART research, training and quality assurance activities, and for the derivation of embryonic stem cells. These procedures cannot occur under the current legislation because of the requirements to first declare an embryo as an excess ART embryo and then complete 'proper consent' procedures. When the research involves damage or destruction of the embryos, 'proper consent' must allow a two-week cooling-off period, during which time those responsible for the embryo can withdraw their consent.

Under current arrangements, embryos that are not suitable for implantation for any reason, including embryos that are found to have a genetic disease using preimplantation genetic diagnosis, are allowed to die and are not available for research. However, ART researchers and practitioners told the Committee that such embryos would be a useful source of fresh (albeit unsuitable for implantation)

embryos for research, training and quality assurance activities. Embryonic stem cell researchers would also like to generate stem cells from embryos carrying genetic defects (eg after pre-implantation genetic diagnosis) to study the cause and treatment of genetic diseases.

It appeared to the Committee that the RIHE Act is not clear on whether such embryos could ever be considered to be 'excess ART embryos' (because they are not suitable for reproductive use in the first place), and therefore whether they could ever lawfully be used for research purposes (even if they are first frozen). In Victoria, this ambiguity is removed because freezing embryos that are not suitable for implantation is prohibited under the Victorian *Infertility Act 1995*. However, this is not the case in other States and Territories.

In view of these ambiguities in the Act, as well as the potential use of embryos that are not suitable for implantation in research, training and quality assurance activities, the Committee considers that there should be clear and unambiguous provisions within the legislation and licensing arrangements for declaring embryos that are unsuitable for implantation as 'surplus embryos', and that such embryos should be permitted to be used for research, training and improvements in clinical practice. However, the Committee acknowledges that, although in some cases the suitability for implantation is an objective decision (eg when the embryo has been diagnosed by PGD to carry a genetic disorder), in other cases it may be subjective (eg when the embryo appears less healthy). Therefore, the Committee's view is that objective criteria should be developed by an expert body, for use in determining whether an embryo is unsuitable for implantation. These criteria could include embryos that have not undergone cell divisions, carry additional pronuclei or show other major chromosomal defects.

Consent arrangements for the use of fresh embryos are discussed in Section 11.2.

Recommendations — use of fresh ART embryos

20. An expert body should formulate objective criteria to define those embryos that are unsuitable for implantation.
21. Fresh ART embryos that are unsuitable for implantation, as defined by the objective criteria, should be permitted to be used, under licence, for research, training and improvements in clinical practice.
22. Fresh ART embryos that are diagnosed by preimplantation genetic diagnosis (according to the ART guidelines) as being unsuitable for implantation should be permitted to be used, under licence, for research, training and improvements in clinical practice.

Somatic cell nuclear transfer

The Committee heard that research using excess ART embryos, under licence, since 2002 has yielded a number of new embryonic stem cell lines, and that researchers are working with these to refine the methods of cell culture and differentiation that will be needed to develop cellular therapies. However, the Committee also heard from those involved in the field that further development of this area of research requires the creation of human embryo clones to generate embryonic stem cells that are either patient-matched for development of specific cellular therapies, or of known genotype for disease modelling and other research (so-called therapeutic cloning).

Furthermore, although much publicity to date has been attached to the use of embryonic stem cells to develop cellular transplantation therapies, the Committee noted that, based on the submissions of experts working in the field, embryonic stem cells have potentially useful applications in other areas of medical research, such as for studying cell differentiation in healthy and diseased tissues (disease modelling studies) and for drug screening. Such studies could increase understanding of disease

processes and lead to cures for diseases through other means apart from cellular therapies. The Committee's view is that there is scientific merit in the use of embryonic stem cells for this type of research.

The Committee acknowledges the advances that have been made in research into adult stem cells, and that adult stem cells have been used successfully in the treatment of some human diseases, especially bone marrow transplantation. However, to date, the potentiality of adult stem cells, in terms of the number of cell types that can be generated, is still unclear and certainly less than for embryonic stem cells.

The Committee has therefore reached an opinion, based especially on the evidence of experts who work directly in one or both fields of stem cell research (adult or embryonic), that further research involving both adult and embryonic stem cells is required to improve knowledge and to develop effective disease treatments.

The Committee heard that research using human cloning to generate embryonic stem cells is proceeding in several other countries where these technologies are legislatively permitted (eg United Kingdom, South Korea, Singapore) or where no national legislative regulations are in place (eg United States). Therefore, many respondents to the reviews argued that the prohibition of human cloning to generate patient-matched stem cells should be lifted in Australia to allow Australian researchers to continue to contribute to the intellectual and biotechnological developments in this field.

During the reviews, the Committee heard three major objections to the use of somatic cell nuclear transfer (or SCNT) to generate embryonic stem cells (as well as other methods of creating human embryos not involving the fusion of an egg and a sperm). One type of argument, commonly referred to as the 'slippery slope' argument, is that, because the technology is the same as that used for reproductive cloning, allowing cloning to extract stem cells would inevitably lead to its use for reproduction. However, the Committee considers that continuing a ban on reproductive cloning would effectively prohibit the development of human embryo clones beyond 14 days or the birth of a human being using such methods. The Committee therefore rejects the 'slippery slope' argument.

A second argument is that it is wrong to create human embryos to destroy them and extract the stem cells. The Committee agreed that human embryo clones are human embryos and that, given the right environment for development, could develop into a human being. Furthermore, if such an embryo were implanted into the body of a woman to achieve a pregnancy, this entity would certainly have the same status as any other human embryo, and were this pregnancy to result in a live birth, that child would enjoy the same rights and protection as any other child. However, a human embryo clone created to extract stem cells is not intended to be implanted, but is created as a cellular extension of the original subject. The Committee therefore agreed with the many respondents who thought that the moral significance of cloned embryos that are not implanted is linked more closely to their potential for research developments, including the development of treatments for serious medical conditions, than to their potential as a human life.

Furthermore, the Committee noted that the production and destruction of such embryos is not dissimilar to the production and destruction of excess ART embryos, which is permitted by the legislation and widely accepted by society. Thus, to permit one (production and destruction of ART embryos) but not the other (production and destruction of nuclear transfer and other bioengineered embryos) is inconsistent and appears to attach more importance to the treatment of infertility than to the treatment of other serious diseases and conditions that could be helped as a result of this activity. In view of the wide range of diseases and conditions that stem cell research aims to help, the Committee considers that further research using cloned human embryos should be permitted.

Thus, the Committee concludes that the creation of human embryos by nuclear transfer should be permitted, under licence, according to strict regulatory guidelines, including strong ethical guidelines for egg donation (see Section 11.2) because:

- While reproductive cloning aims to copy a person, SCNT only aims to copy a person's cells; therefore, provided the person consents, there is no objection to this.
- In addition, if the embryo created by SCNT is not intended to be implanted, it does not represent a potential new individual in the way that the product of fertilisation does.
- After nuclear transfer, the new cell needs to develop to the blastocyst stage so the inner cell mass can be removed, and while this entity is indistinguishable from other types of human embryos, it has been created specifically for research purposes (which is currently prohibited under the PHC Act).
- However, this type of embryo is not intended to be implanted, so the production and destruction of such an embryo is not dissimilar to the production and destruction of excess ART embryos, which is permitted by the legislation and accepted by society.
- Therefore, if research on excess ART embryos is permitted, it is not a major additional step to permit SCNT.

However, a significant argument raised by many respondents against the use of SCNT was that it requires the use of donated human eggs. This raises concerns, because ovarian stimulation and egg collection are associated with more risk than the removal of other tissues for research. Because the 'best' eggs are those from young women, there is also potential for young women to be coerced to donate (such as by payment, through their work or by their families). In this regard, the Committee considers that strict ethical guidelines for obtaining egg donations should be developed and that further research should aim to identify alternative sources of eggs (see Section 17.7). In addition, the Committee considers that the need for human egg donations could be reduced in the early stages of the development of this technology by permitting, under licence, human nuclear transfer into animal egg cytoplasm for the purpose of stem cell research.

The Committee also notes that the majority report of the House of Representatives Standing Committee on Legal and Constitutional Affairs inquiry, chaired by the Mr Kevin Andrews MP in 2001[45], recommended a three-year moratorium on human cloning to extract embryonic stem cells ('therapeutic cloning') rather than a permanent ban.

45. House of Representatives Standing Committee on Legal and Constitutional Affairs (2001). *Human Cloning: Scientific, Ethical and Regulatory Aspects of Human Cloning and Stem Cell Research*, Parliament of the Commonwealth of Australia, Canberra (Andrews Report). http://www.aph.gov.au/house/committee/laca/humancloning/contents.htm

Recommendations — use of human embryos created by somatic cell nuclear transfer

23. Human somatic cell nuclear transfer should be permitted, under licence, to create and use human embryo clones for research, training and clinical application, including the production of human embryonic stem cells, as long as the activity satisfies all the criteria outlined in the amended Act and these embryos are not implanted into the body of a woman or allowed to develop for more than 14 days.
24. In order to reduce the need for human oocytes, transfer of human somatic cell nuclei into animal oocytes should be allowed, under licence, for the creation and use of human embryo clones for research, training and clinical application, including the production of human embryonic stem cells, as long as the activity satisfies all the criteria outlined in the amended Act and these embryos are not implanted into the body of a woman or allowed to develop for more than 14 days.

Use of human embryos created by activation methods not involving fertilisation of a human egg by a human sperm or SCNT

As discussed in Section17.3, the Committee considers that development of a human embryo created by any method not involving the fertilisation of a human egg by a human sperm beyond 14 days, or implantation of such an embryo into the body of a woman, are important prohibitions to ensure that such embryos are not used for reproductive purposes. However, the Committee proposes that a range of practices involving creation of human embryos by methods other than fertilisation should be allowed, under licence. The Committee considers that all nuclear and pronuclear transfer methods (including transfer of stem cell nuclei) should be permitted, under licence, for similar reasons to those already outlined for SCNT above. Similarly, parthenogenetic activation of oocytes should be permitted to allow oocyte maturation research (see above) and for other research and training activities.

Finally, the Committee considered that research involving the use of embryonic precursor cells and gene technology should also be permitted, under licence, to advance knowledge and develop therapeutic applications.

Recommendations — use of human embryos created by activation methods not involving fertilisation of a human egg by a human sperm or somatic cell nuclear transfer

25. Creation of human embryos and human embryo clones by means other than fertilisation of an egg by a sperm (such as nuclear or pronuclear transfer and parthenogenesis) should be permitted, under licence, for research, training and clinical applications, including production of human embryonic stem cells, as long as the research satisfies all the criteria outlined in the amended Act and these embryos are not implanted into the body of a woman or allowed to develop for more than 14 days.
26. Creation of human embryos using the genetic material from more than two people, or including heritable genetic alterations, should be permitted, under licence, for research, training and clinical applications, including production of human embryonic stem cells, as long as the research satisfies all the criteria outlined in the amended Act and these embryos are not implanted into the body of a woman or allowed to develop for more than 14 days.
27. Creation of embryos using precursor cells from a human embryo or a human fetus should be permitted, under licence, for research, training and clinical applications, including production of human embryonic stem cells, as long as the research satisfies all the criteria outlined in the amended Act and these embryos are not implanted into the body of a woman or allowed to develop for more than 14 days.

17.5 Definition of a human embryo

During the reviews, the Committee learnt that different people and groups hold differing views about the meaning and use of the term 'embryo', both in medical science and as a more general term.

The Committee considers that it is essential that the terminology used in the legislation is biologically accurate, clearly understandable by all stakeholders, and unambiguous to regulators, scientists and the public. Therefore, the Committee has taken the view that a very broad biological definition of 'human embryo' should be retained in the Act. This definition covers all stages of development commonly understood by the term 'embryo' in either scientific–medical or public–ethical contexts. The committee suggests, however, that while it is critical to be clear about the terminology used, definitional clarity will not, in itself, resolve moral concerns and it is likely that, whatever language is used, different moral interpretations will be made regarding the status of such entities and the obligations owed to them. The recommendations of the Committee are an attempt to take account of all these views.

As discussed in Section 17.4, the current definition of an embryo sets the starting point of embryonic development as the appearance of two pronuclei. This definition is not based on any precise previous scientific or community definition of an embryo; the Committee was advised that this definition was a compromise between different views and resulted from the legal imperative to have a defined point against which legal judgments could be made. However, the Committee considers that the two pronuclei stage does not represent the formation of a new genetic entity and the use of this definition has had the unintended consequence of impeding or stopping significant areas of ART research (see Chapter 8).

The Committee considers that syngamy is a better definitional starting point for embryonic development because it is at this stage, when the maternal and paternal chromosomes align, that a new genetic entity is formed. However, because the precise point of syngamy is hard to observe in live embryos, the Committee proposes that the definition should refer to the first cell division. Practically, this change would mean that, for example, the biological marker of formation of pronuclei could once again be used as a readily observable marker for fertilisation, which would facilitate ART research on improved methods for treating infertility. This would still prohibit the creation of embryos using human eggs and human sperm for research purposes. Furthermore, this change is consistent with the conclusion of a discussion paper prepared by the National Health and Medical Research Council (NHMRC) on the biological definition of the human embryo.[46]

For embryos created by means other than by fertilisation of a human egg by a human sperm, the NHMRC discussion paper suggests that potential for implantation and future development to a live birth[47] could provide a useful criterion for considering whether such an entity should be included in the definition of a human embryo or not. This criterion was not applied to embryos created by fertilisation, however, because it was considered that all entities created this way should be defined as human embryos, regardless of any chromosomal or other anomalies that may prevent them from future development. These issues are discussed in more detail in Section 8.3.

The Committee considered these issues and has proposed a revised definition of a human embryo, based on the findings of the NHMRC discussion paper.[2] In recommending this change, the Committee considers that the revised definition corresponds with the broadest public understanding of a 'human embryo', as expressed by the community groups who made representations during the review process.

46. *Discussion Paper: Human Embryo — A Biological Definition* (NHMRC December 2005)
47. Where such potential is defined by the appearance of the 'primitive streak' (see Glossary)

The Committee acknowledges that obtaining a licence should be a prerequisite for conducting any research with human embryos but considers that this would not be an unreasonable burden for researchers as the Committee's recommendations will allow research that has previously been prohibited.

Recommendation — definition of a human embryo

28. The definition of a 'human embryo' in both Acts should be changed to:

'A human embryo is a discrete living entity that has a human genome or an altered human genome and that has arisen from either:

(i) the first mitotic cell division when fertilisation of a human oocyte by a human sperm is complete; or

(ii) any other process that initiates organised development of a biological entity with a human nuclear genome or altered human nuclear genome that has the potential to develop up to, or beyond, 14 days

and has not yet reached eight weeks of development.'

17.6 Consent for embryo research

The Committee was mindful of the care and thought that has gone into the development of the NHMRC National Statement[48] and ART Guidelines.[49] It is essential that practices of consent are consistent across different areas of research and clinical practice. However, new areas of research generate situations that may not have been fully envisaged when guidelines are developed and therefore the Committee considers that the NHMRC should review certain aspects of those guidelines.

Donors of excess ART embryos expressed concerns that the current process for declaration of embryos as excess ART embryos, followed (at a later stage) by consent for a specific research project, is unnecessarily drawn out and stressful. In particular, the second stage of the process, when researchers approach embryo donors for consent to a specific research project, can occur some time (possibly many years) after the initial in-principle agreement to research. This reopens the emotional issue of the fate of the embryos. ART consumers advocated a simplification of the process. However, the Committee noted that there are important distinctions between different purposes or intent of the research that are not known until the embryos are selected for a specific project. Furthermore, some people may wish to be involved in the decision about the particular type of research for which their embryo is used, while for others this may not be the case.

In view of the concerns of ART consumers, the Committee's view is that the NHMRC Australian Health Ethics Committee (AHEC) should review its guidelines for consent in these circumstances. In particular, the Committee considers that AHEC should develop arrangements to facilitate donation of 'excess embryos' to research without further contact at a later stage for those who wish to accept this option (with the involvement of human research ethics committees to determine circumstances where this can occur). These arrangements should take into account any preference of those who donate embryos or gametes for the creation of embryos for the type of research for which the tissue will be used.

48. *National Statement on Ethical Conduct in Research Involving Humans* (NHMRC 1999)
see http://www.nhmrc.gov.au/publications/synopses/e35syn.htm
49. *Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research* (NHMRC 2004)
see http://www.nhmrc.gov.au/publications/synopses/e56syn.htm

However, there is a significant difference between research with human embryos for the purposes of improving ART services (where there is no ongoing, live biological material produced from the embryos), and research with human embryos for the purpose of creating embryonic stem cell lines that are 'immortal' and will be used in various other ongoing research contexts. In this regard, the Committee considers that it is necessary for consent to be obtained and that it is important for people to be fully informed about the commercial potential of their donation and, where possible, appropriate conditions should be put in place for personal use of any products of the research by the donors (such as for the treatment of children who are matched with any stem cell lines derived).

Finally, to facilitate the use of 'surplus' or unfit embryos (including PGD embryos) for research or training, the Committee considers that AHEC should also develop guidelines for consent in these circumstances.

Recommendations — consent arrangements for the donation of embryos

29. The NHMRC should review its guidelines in relation to consent to research on excess ART embryos, in order to clarify the consent process in relation to the following issues:
    - the circumstances, if any, where those who choose to donate excess ART embryos to research may be able to choose not to be contacted at some later stage to give consent to a particular research proposal
    - the circumstances, if any, where a human research ethics committee can determine that the researcher need not ask for further consent to use embryos already declared 'excess'
    - the development of an appropriate form of consent that could be completed by the responsible persons for excess ART embryos shortly after the declaration that the embryos are excess
    - the manner in which those who donate embryos or gametes for the creation of ART embryos may express any preference for the type of research for which the tissue will be used, once the embryo is declared excess.

30. The NHMRC should develop ethical guidelines for the use of embryos that are unsuitable for implantation for research, training and improvements in clinical practice (see Recommendations 20–22).

17.7 Egg donors

The Committee is concerned that changing the legislation to permit nuclear transfer and related technologies would lead to an increased demand for donated eggs (oocytes). The only oocytes presently available for research would be those donated by young women, and the Committee is concerned that this could lead to exploitation of these women. The Committee also noted that oocyte donation for research purposes raises particularly salient ethical concerns, because donors receive no direct medical benefit but are exposed to an increased risk of morbidity or mortality associated with the follicle stimulating hormone treatment required for mature egg retrieval. In addition, the Committee notes with concern the recent publicity about research overseas involving unethical inducement of research staff to donate eggs.[50] In the light of this, the Committee's view is that firm guidelines should be prepared to ensure that egg donors give free consent, and have all the appropriate information, including whether or not the eggs may be used to make embryos for research purposes.

50. Editorial (2005). Will the regulator please stand up. *Nature* 438(7066):257

The Committee is concerned that women in ART treatment programs may be requested to donate eggs for research and, therefore, to avoid coercion of women in this situation, considers that there should be a clear separation between the obtaining of eggs for ART practice and research. Coercion of other vulnerable people (such as research assistants) and living, related donors should also be discouraged by strict guidelines for preventing or restricting such activities.

The Committee heard the view that the level of reimbursement made to egg donors should be substantial to compensate for the risks. However, the Committee formed the view that payment to donors should not be permitted beyond reimbursement of reasonable expenses, in order to limit the risk of exploitation of women and commodification of tissue.

The Committee considered other ways in which eggs could be obtained, such as after surgical removal of ovaries for conditions such as cancer or polycystic ovary disease, or cadaveric donation (as with other organ donation). Use of such material would avoid the need for individual egg donations.

Finally, the Committee heard of several avenues of research that would overcome the need for eggs in embryonic stem cell research, such as the production of eggs from stem cells in culture or the use of stem cell cytoplasm to incubate adult cell nuclei. Further research on maturing oocytes in the laboratory, and freezing of mature eggs, would also reduce the need for hormone stimulation of women making individual donations of mature eggs. The Committee's view is, therefore, that these lines of research should all be encouraged to overcome the need for donation of mature eggs as soon as possible. In addition, the Committee has also already suggested that nuclear transfer using animal eggs could be permitted for limited research purposes to establish proof of principle and reduce the need for human egg donation (see Section 17.4).

Recommendations — egg donation

31. The current principles of consent for participation in medical research must apply to sperm, egg and embryo donors, so as to ensure that decisions are freely made.
32. The NHMRC should develop guidelines for egg donation.
33. The present prohibition of the sale of sperm, eggs and embryos should continue, but the reimbursement of reasonable expenses should continue to be permitted.

17.8 Licensing arrangements

Current arrangements

Respondents to the reviews from all stakeholder groups, including researchers, were supportive of the need for strong regulatory oversight of this type of research. The Committee considers that the Licensing Committee fulfils a valuable role in this process and is broadly supported by researchers and by the community.

The Committee notes that delays in issuing of the first licences were an unavoidable consequence of the processes to establish the new regulatory system in this complex area of legislation. As indicated in Recommendations 14–27 above, the Committee's view is that the role of the Licensing Committee should be expanded to include licensing of the additional activities that the Committee has recommended, including creation of human embryo clones by nuclear transfer, parthenogenetic activation of oocytes, experimental fertilisation, and other related research, training and quality assurance activities. However, the Committee notes that institutional human research ethics committees are able to allow or decline specific research proposals for their own institutions.

However, these delays, as well as a lack of clarity in some aspects of the application process, were seen by researchers as inhibiting research, training and quality assurance activities. Conversely, some nonresearchers thought that the licensing process had not been sufficiently rigorous, although the Committee noted that this was, to some extent, due to a lack of public understanding of the licensing requirements (see Section 9.2). The NHMRC itself has observed that there are deficiencies in the legislation relating to the operations of the Licensing Committee, and that amendments to the legislation could improve the efficiency and clarity of the process.

The Committee heard that, due to the specific expertise of each Licensing Committee member, a vacancy on the committee poses a significant problem, because licensing applications cannot be handled effectively. As appointment to the committee involves approval by all States and Territories, there have been lengthy delays in filling vacancies. The Committee noted that there is not scope in the Act as presently framed to address this problem, which is because the Licensing Committee is a national committee that oversees research in all States and Territories. The Committee therefore draws this to the attention of the Australian Parliament and the Council of Australian Governments for consideration and recommends that they give urgent attention to this problem.

The Committee considered that delegation of the powers of the chair, powers to suspend and revoke licences, and other practical issues raised, could be managed under the RIHE Act s15. Similarly, the Committee considered that the issuing of joint licences was a matter for the Licensing Committee to decide, with legal advice, if necessary.

A further area of concern for the Licensing Committee was the need to receive feedback on research outcomes (such as for the derivation of stem cell lines) to inform further decisions relating to whether such research represents a 'significant advance in knowledge or improvement in technology'. The Committee's view is that the Licensing Committee should request reports from researchers using embryonic stem cells derived from licensed activities, and for a reasonable period beyond the conclusion of the licence, as a condition of the issuing of a licence, similar to reporting to HRECs, as a condition of the licence (RIHE Act s24).

The Committee supports the role of the HRECs and the two-stage system of approval of research, with initial approval by the local HREC followed by application for a licence from the Licensing Committee.

The cost of supporting the Licensing Committee and the national compliance system was $3.3 million in 2003–04. To date, no cost-recovery mechanism has been applied to recover these costs (see Section 9.1). However, due to the low number of licences issued, cost recovery from licence applicants would be exorbitant In addition, research organisations already meet the considerable costs of compliance with the national regulatory scheme, including licensing requirements. The Committee's view is that, if cost recovery were to be pursued, it would be likely that research would be severely limited.

Recommendations — licensing arrangements

34. The Embryo Research Licensing Committee of the NHMRC (the Licensing Committee) should continue to be the regulatory body responsible for assessing licence applications, issuing licences and monitoring compliance, as under current arrangements.
35. The role of the Licensing Committee should be extended to include assessment of licensing applications and issuing licences for any additional activities permitted, under licence (see Recommendations 14–27).
36. The Australian Parliament and the Council of Australian Governments should give urgent attention to the problem of delays in the filling of vacancies on the Licensing Committee.
37. There should be no attempt to recover the cost of administration, licensing, monitoring and inspection activities associated with the legislation from researchers at this point in time.

17.9 Monitoring and compliance

The Committee heard that, under the arrangements set out in the RIHE Act, the Licensing Committee chair has appointed inspectors, and a monitoring and inspection system for facilitation and monitoring compliance with the legislation has been set up and is generally regarded as suitable.

However, the Committee also heard from the Licensing Committee and others that there is a major deficiency in the legislation with regard to the limited powers of the inspectors appointed under the RIHE Act to monitor activities that are not covered by a licence. As a result of this deficiency, suspected breaches by non-licence-holders, including suspected breaches under the PHC Act, cannot be adequately investigated. In terms of licensed premises, the Committee also heard that inspectors do not have the power to make unannounced inspections, which also inhibits their ability to investigate suspected breaches.

The Committee's view is that inspectors should have adequate powers under both Acts to investigate suspected breaches of either Act. There is a legal question whether these powers already clearly exist, notwithstanding s41 of the RIHE Act. The Acts should be amended accordingly if this is necessary.

Recommendations — monitoring powers

38. The Licensing Committee should continue to perform its functions in relation to licences and databases for research permitted by licences under the RIHE Act.

39. Licensing Committee inspectors should be given powers, under the PHC and RIHE Acts, of entry, inspection and enforcement in relation to non-licensed facilities in the same manner and by the observance of the same procedures as applicable to search warrants under Commonwealth legislation, if such powers do not clearly exist.

17.10 Oversight of ART clinical practice and research

Under the RIHE Act, the creation and use of human embryos for ART can only be carried out by an accredited ART centre, defined in the RIHE Act and current RIHE Regulations as a centre accredited by the Reproductive Technology Accreditation Committee (RTAC) of the Fertility Society of Australia. During the reviews, the Committee received information about this accreditation system, which involves accreditation by RTAC against a code of practice developed by the industry (RTAC Code 2005).

Most respondents regarded the current arrangements for oversight of ART services by national and State or Territory bodies as appropriate and effective. There appears to be a cooperative relationship between RTAC, at the national level, and statutory bodies established at the State level. Advantages to the RTAC self-regulatory model include its flexibility to respond to technological change, and its inclusion of a wide range of professional and consumer interests. However, at least in some States, there may be some potential for confusion about the various requirements in legislation, guidelines and codes of conduct.

The Committee received a few comments arguing against industry self-regulation. However, it also received strong endorsement of the current arrangements by ART consumers and heard that ART consumer representatives have been represented on the RTAC Accreditation Board and involved in the development of the RTAC Code 2005.

The Committee noted that an important aspect of the accreditation arrangements is that the ART Guidelines 2004 are mandated in the RTAC Code 2005, a system that ensures compliance with these guidelines, including adherence to the arrangements for declaring ART embryos to be excess and for

proper consent for donation of embryos for research. The latter arrangements are also included in the statutory arrangements under the RIHE Act (ss8 and 24). The Committee formed the view that these arrangements are effective and should continue.

Recommendation — oversight of ART clinical practice and research

40. There should be a continuation of the role of the Reproductive Technology Accreditation Committee in the regulation of ART.

17.11 Import and export of human reproductive materials for personal use

During the reviews, the Committee heard that controversy around trade and international exchange of gametes, embryos and embryonic stem cells is related to ethical concerns about the sources and uses of these materials, the commodification of human tissues, and the commercialisation of any therapeutic products derived from them.

However, the Committee heard from ART consumers that the current export prohibitions and custom regulations regarding human embryos have made it difficult for couples to export their embryos overseas for their own reproductive use. The Committee's view is that the current arrangements, which involve personal application to the Minister for Customs to export embryos for personal reproductive use, are too cumbersome and stressful for users and should be streamlined.

Recommendation — import and export of human reproductive materials for personal use

41. The import or export of a patient's reproductive material, including ART embryos, for the purpose of that person's ongoing ART treatment should not require any regulation other than that required under existing quarantine regulation.

17.12 Trade and international exchange of human reproductive materials for research use

The PHC Act bans the creation, import and export of human embryo clones, but the import of material derived from human embryo clones (or from any embryos), such as embryonic stem cell lines, is covered by aspects of the Customs Act and Regulations, which prohibit the import of any products of prohibited embryos. However, products that comply with Australian requirements (such as embryonic stem cell lines obtained, under licence, from excess ART embryos) can be imported (under conditions overseen by the Australian Quarantine and Inspection Service).

The Committee heard from some researchers that these arrangements had not affected their research, whereas others noted the importance of Australian researchers having access to further cell lines from overseas. There was general concern about whether such imported cell lines have been derived using

practices consistent with Australian legislation. The Committee's view is that the existing requirements for the import and export of human biological materials are satisfactory for ethically derived human embryonic stem cells.

Recommendations — trade and international exchange of human reproductive materials and stem cells

42. The import or export of ethically derived viable materials from human embryo clones should be permitted after approval by the appropriate authority.
43. The existing requirements for the import and export of human biological materials are satisfactory and, for ethically derived human embryonic stem cells, no further restrictions are necessary.

17.13 Biotechnology and commercialisation

There is a strong view that gametes and embryos should not be commodified by permitting people to sell their own gametes and embryos. Respondents were also concerned to see the benefits of altruistic donation translated into public benefit and access to therapeutic applications arising from the research. However, the Committee also notes that stem cell technology is regarded as a useful platform for investment by the biotechnology industry and understands that such investment is needed to develop potential therapies. This would require that the products of the research and development activities are able to be commercialised.

The Committee's view is that there is a necessity to balance commercial interest with recognition of altruistic donation. The Committee strongly supports the current system of monitoring by HRECs to ensure informed consent processes.

Recommendations — biotechnology and commercialisation

44. Trade in human gametes or embryos, or any commodification of these items, should continue to be prohibited.
45. Donors of tissue that is going to result in an immortal stem cell line should be informed by means of processes monitored by human research ethics committees about the potential use of that stem cell line, including the potential for commercial gain and the fact that they may not have any rights in potential stem cell developments.
46. The development of biotechnology and pharmaceutical products arising from stem cell research should be supported.

17.14 The applicability of a national stem cell bank

Stem cell banks offer a way of facilitating research by making the stem cell lines more widely available to the international research community. Other living tissues already banked in Australia for use in transplantation medicine include heart valves, bone, skin, and cord blood. There are also numerous research tissue banks, including banks for various tumour samples and banks for specific diseases and for specific organs.

There are now a number of stem cell registries around the world holding information about the source, characteristics and derivation of stem cell lines, and a number of stem cell banks are either active or planned. The UK Stem Cell Bank, funded by the UK's Medical Research Council and Biotechnology and Biological Sciences Research Council, began operating officially in January 2003 and two Australian embryonic stem cell lines have already been accepted into it.

Although some scientific researchers argued that an Australian stem cell bank may not be necessary because overseas stem cell banks (eg the UK cell bank) were adequate, the Committee heard overall strong support for an Australian national stem cell bank in order to provide improved access to stem cell lines for research and to provide a quality control mechanism for stem cell research. Different models for the administration of a national stem cell bank were suggested. Some recommended that a national stem cell bank be established at the major national research facility at the Australian Stem Cell Centre (ASCC), which is already capable of storing stem cell lines. Other suggestions were that a national stem cell bank be based on the UK Stem Cell Bank, that such a bank be a decentralised structure incorporating 'nodes' of specific research interest or expertise located in different parts of the country, or that a registry of stem cells would be a better system.

Fair access and equal involvement were the two main concerns about community involvement in a national stem cell bank. There was concern about the potential for exploitation of stem cells from minority groups. Some respondents were also concerned that the driving force behind a national stem cell bank was commercial rather than scientific or medical. While the Committee acknowledged that commercialisation of therapeutic products would be an outcome of stem cell research, it also came to the view that stem cell banks would help to keep research resources in the public domain.

Some respondents commented that a stem cell bank would be expensive to maintain. The Committee has not investigated the financial implications of operating a stem cell bank. However, financial support for this activity would be essential if the stem cell lines are to be made available to the scientific community.

The Committee's view is that an Australian national stem cell bank would make stem cells, including embryonic and adult stem cells, more widely available to researchers and also limit the number of embryos required for further derivation of stem cell lines. As the Australian Stem Cell Centre already has a stem cell banking facility, the Committee considers that this facility could be expanded to accommodate a national bank administered by ASCC. However, ASCC should liaise closely with other stem cell banks overseas and use compatible operating principles.

Many respondents, including both ART consumers and ART clinics, were concerned that, following the decision to make excess ART embryos available for research, there would be no opportunity for these embryos to be used in actual research projects. One IVF clinic suggested that a national embryo bank should be established in conjunction with a national stem cell bank to allow more couples to donate their excess ART embryos for research. It was the Committee's view that such an embryo bank may not have broad community support. However, the Committee considered that there would be considerable potential in the establishment of a national register of donated embryos. This register could be maintained by the Licensing Committee if empowered to do so. This register may serve the function of facilitating embryo donation for research and would provide a transparent account of the number of donated excess ART embryos held. It may also be possible that such a register may facilitate embryo donation to another couple.

Recommendations — national stem cell bank

47. A national stem cell bank should be established.
48. Consideration should be given to the feasibility of the Australian Stem Cell Centre operating the stem cell bank.
49. A national register of donated excess ART embryos should be established.

17.15 Regulatory approach to legislation

The Committee noted that both the proponents and opponents of human embryo research would prefer to have legislation in this area, rather than to have no specific regulation. However, the Committee also heard a number of concerns about the capacity of legislation to respond to research needs in a fast-moving area of technology. These included difficulties in anticipating advances in knowledge and potential new uses of the technology, ambiguities and difficulties in interpretation, and unfair exposure of researchers to potential prosecution (see Chapter 16 for further discussion of these issues).

The Committee's view is that some activities should remain entirely prohibited, in order to assuage community concern that practices that are widely condemned will be prohibited. At present, these activities are set out in the PHC Act and include reproductive cloning, creating a human embryo other than by fertilisation, placing certain types of embryos in a woman's reproductive tract and other related offences (see Section 17.3).

To increase certainty and flexibility in the application of the legislation, especially in face of rapidly changing technology, the Committee's view is that the Licensing Committee should be authorised to give rulings on the interpretation of the provisions creating offences under the PHC Act, with a statutory requirement that the Committee must report immediately in detail to the NHMRC and to parliament on its rulings. As with rulings given by the Commissioner of Taxation, people who act on the basis of such rulings should have statutory immunity from prosecution.

In relation to activities that are permitted with a licence under the RIHE Act, the Committee recommends that the Licensing Committee should be empowered to give a ruling that enables it to grant a licence for an activity that may fall outside the literal wording of the Act but seems to fall within its general tenor. If the Committee gives such a ruling, it should be required to report immediately in detail to the NHMRC and to parliament on that ruling and any licence granted on the basis of the ruling. Again, there should be statutory protection for those who act in good faith on such advice.

The Licensing Committee's authority to provide rulings on the interpretation of provisions of both Acts should be specified in those Acts. Section 41 of the RIHE Act appears to give the Licensing Committee powers under both Acts; but, to remove any doubt, it would be preferable for the requisite powers to be specifically conferred under both Acts.

The Committee notes that there are precedents for this approach in other areas of law, such as taxation (where the Commissioner for Taxation can issue 'rulings' on the applicability and interpretation of various taxation legislation). Also, such an approach would complement the monitoring and compliance procedures that have been set up by the licensing inspectors to assist researchers to comply with the law, and with prosecution seen as an action of last resort (see Chapter 10).

The Committee has not come to any view about whether the two Acts should remain separate or be incorporated into one because, in its view, this is a matter for parliament. However, the Committee notes that the more flexible regulatory arrangements it has recommended would reduce the need for an ongoing review process. Nevertheless, in view of the fast moving developments in the field and the range of amendments proposed in these reviews, it is the Committee's view that the two Acts should be subject to a further reviews, either six years after royal assent of the PHC and RIHE Acts or three years after royal assent to any amended legislation.

Recommendations — regulatory approach to legislation

50. The Licensing Committee should be authorised under the Prohibition of Human Cloning Act to give binding rulings on the interpretation of that Act, or the regulations made under that Act, on condition that it reports immediately and in detail to the NHMRC and to parliament on such rulings.
51. The Licensing Committee should be authorised by the Research Involving Human Embryos Act to give binding rulings and to grant licences on the basis of those rulings for research that is not within the literal wording of the Act, or the regulations made under the Act, but is within their tenor, on condition that the Committee reports immediately and in detail to the NHMRC and to parliament on any rulings it gives, or any licences it grants, in that way.
52. A researcher who conducts research on the basis of a ruling or a licence should be protected from liability under the legislation, provided that they act in accordance with the relevant ruling or licence.
53. In view of the fast moving developments in the field, and the range of amendments proposed herein, the two Acts should be subject to a further review either six years after royal assent of the current Acts or three years after royal assent to any amended legislation.

17.16 Education and public awareness

The Committee found that public knowledge of stem cell research and ART research was limited. A number of respondents expressed surprise and concern about the use of excess ART embryos for ART research and clinical training, because they had formed an opinion based largely on media reports that these Acts were to regulate embryonic stem cell research.

The Committee noted that the scientific community and the public (informed by the media) frequently underestimated the likely timeframes for translation of research activity into therapeutic outcomes and that this may lead to disappointment and diminished public trust. The Committee therefore suggests that accurate presentation and reporting of research advances is critical for public engagement with this area of research. In particular, emphasis should be given to making realistic assessments of the short-term and long-term benefits of the research.

The Committee noted the current work on stem cell education and endorsed these programs. However, further public education and consultation programs are needed to enable appropriate engagement and understanding of these fields of research and their application. The Committee's view is that the NHMRC, through the Licensing Committee, could play a role in this process.

Recommendation — public education

54. There should be ongoing public education and consultation programs in the areas of science that are relevant to the Acts.

Appendixes

Appendix 1 Committee membership

Legislation Review Committee

Chair	The Hon John S Lockhart AO QC
Members	Associate Professor Ian Kerridge (NSW)
	Professor Barry Marshall (WA)
	Associate Professor Pamela McCombe (Qld)
	Professor Peter Schofield (NSW)
	Professor Loane Skene (Vic)

(See below for further details on the committee members.)

Independent secretariat

Manager	Mr Robert Diamond, Secretariat Australia
Secretary	Dr Andina Faragher, Secretariat Australia
Technical writing	Dr Janet Salisbury and team, Biotext
Administrative support	Ms Jaime Diamond, Secretariat Australia

Media management and public relations

Advisor	Ms Kay McNiece, McNiece Communications

Committee members

The Hon John S Lockhart AO QC (Chair)

The Honourable John Lockhart is a highly regarded member of the international legal community. He was a Justice of the Federal Court of Australia from 1978 until 1999. He has been a member of the Appellate Body of the World Trade Organization, Geneva, Switzerland since 2002 and was appointed as the Deputy Chair of the International Legal Services Advisory Council in 2004. Mr Lockhart has highly relevant experience in chairing high level committees that deliberate on contentious issues.

Associate Professor Ian Kerridge (New South Wales)

Associate Professor Kerridge is a highly regarded clinical ethicist and specialist haematologist. He is Associate Professor in Bioethics and Director of the Centre for Values, Ethics and Law in Medicine at the University of Sydney and Staff Haematologist/Bone Marrow Transplant Physician at Westmead Hospital, Sydney. Associate Professor Kerridge has highly relevant skills and expertise demonstrated through his work and publications in the fields of health ethics.

Professor Barry Marshall (Western Australia)

Professor Marshall is Research Professor of Microbiology at the University of Western Australia and also brings generalist scientific expertise in addition to his abilities in community representation. He is a highly awarded scientist of international renown who is also a successful community advocate both in Australia and overseas. He is a specialist gastroenterologist who is noted for his discovery of the link between the bacteria *Helicobacter pylori* and gastric ulcers. Professor Marshall and a colleague won the 2005 Nobel Prize in Physiology or Medicine for this discovery.

Associate Professor Pamela McCombe (Queensland)

Associate Professor McCombe is a Consultant Neurologist and a Visiting Medical Officer at the Royal Brisbane Hospital and holds the position of Associate Professor, Department of Medicine at the University of Queensland. She is Chair of the Wesley Research Institute Research Committee and Chair of the Scientific Program Committee of the Australian Association of Neurologists.

Professor Peter Schofield (New South Wales)

Professor Schofield is a renowned neuroscientist. He is Executive Director and Chief Executive Officer of the Prince of Wales Medical Research Institute, Senior Principal Research Fellow at the Garvan Institute of Medical Research and Conjoint Professor at the Faculty of Science and Faculty of Medicine at the University of New South Wales. Professor Schofield's skills and expertise are in a highly relevant scientific discipline to the review subject matter.

Professor Loane Skene (Victoria)

Professor Skene is a renowned lawyer, ethicist and academic. She is Pro Vice-Chancellor, Professor of Law in the Law Faculty and an Adjunct Professor of Law in the Faculty of Medicine, Dentistry and Health Sciences at the University of Melbourne. Professor Skene has highly relevant skills and expertise demonstrated through her work and publications in the fields of health law and ethics.

Appendix 2 Issues Paper

Legislation Review

Legislation Review of Australia's *Prohibition of Human Cloning Act 2002* and *Research Involving Human Embryos Act 2002*

Issues Paper:

Outline of existing legislation and issues for public consultation

August 2005

Legislation Review Committee

Legislation Review

About this Issues Paper

Welcome to the Legislation Review of Australia's *Prohibition of Human Cloning Act 2002* and *Research Involving Human Embryos Act 2002*.

This Issues Paper has been prepared by the Legislation Review Committee ('the Committee') to:

- provide information about the Legislation Review
- promote community understanding of the current legislation
- highlight some of the main issues where public and stakeholder comment would assist the Committee in making its recommendations.

Please note that the information provided is factual, based on the legislation and regulatory arrangements as they currently stand. To date, the Committee has had very little discussion of the issues covered and has not yet reached any position on them.

Readers of this paper who wish to take part in the consultation are encouraged to read the legislation in full, and other material available on the Legislation Review website (see below) and on the website of the National Health and Medical Research Council (http://www.nhmrc.gov.au/embryos/index.htm).

Have your say

The Committee would like to receive submissions from all organisations and individuals with an interest in the issues covered by the legislation. Instructions for making a submission are on the Legislation Review website.

Contact details for further information and to make a submission:

Legislation Review website:
http://www.lockhartreview.com.au

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Abbreviations

ART	assisted reproductive technology
COAG	Council of Australian Governments
HREC	human research ethics committee
IVF	in vitro fertilisation
NHMRC	National Health and Medical Research Council
PHC Act	*Prohibition of Human Cloning Act 2002*
RIHE Act	*Research Involving Human Embryos Act 2002*
s	section (of Acts)
SCNT	somatic cell nuclear transfer

Summary

In December 2002, the Australian Parliament passed the *Prohibition of Human Cloning Act 2002* and the *Research Involving Human Embryos Act 2002*. The combined effect of the two Acts is to prohibit human cloning and several other practices considered unacceptable, prohibit the creation of human embryos (by any means) for any purpose other than for attempting to achieve a pregnancy in a woman, and allow certain uses of excess human embryos created through assisted reproductive technology (ART) under strict regulation and licence.

In June 2002, through the Council of Australian Governments (COAG), all States and Territories agreed to introduce nationally consistent legislation. Since December 2002, legislation has been passed in South Australia, Victoria, Queensland, New South Wales, Tasmania, the Australian Capital Territory and Western Australia, and is currently being drafted in the Northern Territory.

Both of the Australian Government Acts include a clause requiring that their operation be independently reviewed within three years (that is, by December 2005). An independent committee, the Legislation Review Committee ('the Committee'), has been appointed to conduct the reviews. The six-person committee, chaired by the Hon John Lockhart AO QC, has been appointed by the Australian Government with the agreement of each State and Territory government. The purpose of the reviews is to assess the scope and operation of the existing regulatory framework. It is not the purpose of the reviews to revisit the underpinning community debate and rationale for the legislation. Rather, it is to review the two Acts in light of changes in scientific or community understanding or standards since 2002, and any indications that the provisions are no longer appropriate and/or practical in their application.

Under the terms of reference for the reviews, the Committee must take into account 'community standards', and consult with the Australian Government, the State and Territory governments, and a broad range of people with expertise in, or experience of, relevant disciplines. To meet these requirements, the Committee has publicly called for written submissions from interested parties. The Committee will also meet with representatives of government, research, ART and the community in each State and Territory.

After the consultations are complete, the Committee will prepare a report for each Act with recommendations for amendments (if any). These reports will be submitted to COAG by 19 December 2005 and tabled in both Houses of the Australian Parliament. The Australian Government will consider the findings of the reviews in consultation with State and Territory governments.

This Issues Paper has been prepared by the Committee to increase community understanding of the legislation and provide a basis for written submissions to the reviews. The paper includes background information about the passage of the legislation in 2002 and the Legislation Review, information about some key definitions used in the Acts, and summaries of the two Acts. It also includes a discussion of the regulatory framework for import and export of reproductive materials and stem cells, an outline of the scope of scientific research affected by the legislation and information on overseas legislation. Throughout the paper, some issues are highlighted that are of particular interest to the Committee relating to the terms of reference for the reviews. Interested parties are invited to respond to these issues and to any other issues relating to the scope and practical operation of the two Acts.

1 History of the legislation

During the 1990s, research in assisted reproductive technology (ART) and human stem cells raised some new challenges. New techniques for creating a human embryo became possible, the creation of 'Dolly' the sheep in 1997 raised the possibility that cloning a human may become technically feasible, and research interest in cells taken from inside human embryos (so-called 'embryonic stem cells') increased. These developments raised significant ethical issues about how human embryos can be created, what forms of human reproduction are acceptable, and what research uses of human embryos should be permitted.

In the late 1990s, there was no nationally consistent legislation covering these issues in Australia. Three states (Victoria, South Australia and Western Australia) had introduced legislation relating to ART practice. This legislation prohibited certain practices and regulated research involving embryos and/or eggs and sperm (gametes).

In 1999, a House of Representatives Standing Committee on Legal and Constitutional Affairs inquiry into these issues was set up. The standing committee released its report, *Human Cloning: Scientific, Ethical and Regulatory Aspects of Human Cloning and Stem Cell Research*, in August 2001. After the release of this report, the Council of Australian Governments (COAG) considered the issues in depth. In 2002, COAG agreed that the Australian Government and State and Territory governments should:

- introduce nationally consistent legislation to ban human cloning and some other related practices considered to be unacceptable
- regulate research involving human embryos that had been created for ART treatments but were no longer required for treatment ('excess ART embryos').

The Prohibition of Human Cloning and Research Involving Human Embryos Bill was introduced into the Australian Parliament in June 2002. After initial debate, the Bill was split into two parts. Following further intensive debate, in December 2002, two Acts were passed:

- *Prohibition of Human Cloning Act 2002*
- *Research Involving Human Embryos Act 2002*.

The combined effect of the two Acts is to:

- **prohibit** human cloning and several other practices considered unacceptable
- **prohibit** the creation of human embryos, by any means, for any purpose other than for attempting to achieve a pregnancy in a woman
- **allow** certain uses of excess human embryos created through ART under strict regulation and licence.

Sections 4 and 5 of this Issues Paper provide further information about the legislation and its implementation.

Although there was no national legislation until 2002, national arrangements for accreditation and ethical oversight of ART clinical services and research were in place in the 1990s. These arrangements still apply as follows:

- ART clinical services must be accredited by the Reproductive Technology Accreditation Committee (established in 1987 by the Fertility Society of Australia) against a code of practice developed by the profession
- both ART clinical services, and professional and publicly funded researchers, are expected to comply with National Health and Medical Research Council ethical guidelines.

Section 5 of this Issues Paper includes further information about these arrangements.

State and Territory legislation

Under the COAG agreement, all the States and Territories agreed to introduce nationally consistent legislation into their respective parliaments. Since December 2002, legislation has been passed in South Australia, Victoria, Queensland, New South Wales, Tasmania, the Australian Capital Territory and Western Australia, and is currently being drafted in the Northern Territory.

The Australian Government Acts do not exclude the operation of any State or Territory laws. Rather, they provide a framework for concurrent operation of State or Territory, and Australian legislation.

2 Legislation Review

Each of the Acts includes a clause requiring that its operation be independently reviewed within three years (that is, by December 2005). The Hon Julie Bishop MP, Minister for Ageing (the minister with portfolio responsibility for human cloning and embryo research), has appointed an independent committee — the Legislation Review Committee ('the Committee') — to conduct the reviews. The Committee is chaired by the Hon John Lockhart AO QC and has five other members with expertise in ethics, law, medical practice, science and community representation (see Appendix 1 of this Issues Paper). The appointments have been agreed by each State and Territory.

What is the purpose and scope of the reviews?

The purpose of the reviews is to assess the scope and operation of the existing regulatory framework and to recommend whether the Acts should be amended, and if so, in what way.

Detailed requirements for the reviews are set out in the current legislation and the terms of reference for the Committee (see Appendix 2 of this Issues Paper). They include a number of issues that the Committee needs to consider in order to review the scope and operation of the Acts. It is not the purpose of the reviews to revisit the underpinning community debate and rationale for the two Acts. Rather, the purpose is to review the Acts in the light of any changes in scientific or community understanding or standards since 2002, and any indications that the provisions are no longer appropriate and/or practical in their application.

How will the Committee conduct the reviews?

An important requirement of the terms of reference of the reviews is that the Committee must take into account 'community standards'. The Committee must also consult with the Australian Government, State and Territory governments, and a broad range of persons with expertise in, or experience of, relevant disciplines (see Appendix 2 of this Issues Paper).

To meet these requirements, and also encourage the Australian community to discuss these issues, the Committee has called for submissions from the general public, as well as from governments, individuals and organisations with relevant expertise, and special interest and community groups — anyone, in fact, who has an interest in these issues.

In addition to the written submissions, the Committee plans to meet with representatives of government, research, ART agencies and the community in each State and Territory.

How will the information be used?

Written submissions will be forwarded in full to all members of the Committee who will use them to inform their work to prepare the final reports of the reviews. Selected transcripts will also be posted on the Legislation Review website and material from them may be quoted in the final reports of the reviews. After the consultation has closed, the Committee will consider all the information gathered that is within the terms of reference of the reviews. It will then prepare two reports (one for each Act), which will describe the Committee's findings and make recommendations for amendments (if any) to the Acts. Information provided to the Committee at meetings in each State and Territory will be recorded and also used to inform the Committee in preparation of its reports. The two reports of the Committee will be forwarded to COAG and to both Houses of the Australian Parliament by 19 December 2005, for consideration by the Australian Government, and State and Territory governments.

Who will make the final decision?

The Australian Government will consider the findings of the reviews in consultation with State and Territory governments.

Timeframe for reviews

9 July 2005	Call for submissions Legislation Review website set up
3 August 2005	Issues Paper released
9 September 2005	Closing date for submissions
August — October 2005	State and Territory meetings, hearings and discussion forums
October — November 2005	Consideration of submissions and other information by Legislation Review Committee Preparation of reports
December 2005	Submission of Committee reports to COAG and to both Houses of the Australian Parliament (by 19 December)

3 Some key definitions

The importance of a 'common language'

The *Prohibition of Human Cloning Act 2002* and the *Research Involving Human Embryos Act 2002* include precise definitions of 'human embryo' and 'human embryo clone', around which the legislation and the national regulatory scheme are based. It is therefore important that everyone has the same understanding of these terms and the way that they are currently used in the legislation. Definitions of these terms from the legislation are provided below with an explanation in plain English and a brief discussion of the legal, scientific and public understanding of the terms.

The definition of 'assisted reproductive technology' (ART) is also discussed briefly because, although this term is not specifically defined in the Acts, it is central to the scope and operation of the *Research Involving Human Embryos Act 2002.* (Other definitions are discussed in Sections 4 and 5 of this Issues Paper.)

Neither of the Acts defines stem cells or human stem cells. This is because research on stem cells is not covered by the legislation as such. Although some researchers want access to human embryos to obtain stem cells, the focus of the legislation is on the creation and use of human embryos rather than on embryonic stem cells. However, human stem cell research is likely to be the subject of much discussion for the reviews, and stem cell terminology is difficult and dynamic and continues to be a source of misunderstanding. A brief explanation of stem cell terminology is therefore included in this section.

Human embryo

Definition from legislation

The legislation defines a 'human embryo' as follows:

> A live embryo that has a human genome or an altered human genome and that has been developing for less than eight weeks since the appearance of two pronuclei or the initiation of its development by any other means (not including any period when its development was suspended for any reason). [PHC Act, s 8(1); RIHE Act, s 7(1)]

What does it mean?

A live embryo ...	For an embryo to be defined as a 'human embryo', it must be viable (that is, able to grow and develop).
... that has a human genome	This means that the embryo must have the usual component of human chromosomes containing the blueprint of human development in the form of DNA, organised as genes.
... or an altered human genome	Because modern gene technology can be used to alter genes, this part of the definition says that even if the human genome is genetically altered in some way, the embryo is still considered human.[1]
... and has been developing for less than eight weeks	This means that the developing human organism continues to be defined as an embryo for eight weeks (after which it is defined as a fetus).
... since the development of two pronuclei	When a sperm penetrates an egg cell, the head of the sperm moves across the cell and fuses with the nucleus of the egg. Before fusion, the male and female chromosomes (which are inside the head of the sperm and the egg cell nucleus, respectively) become visible as dense bodies called 'pronuclei', which move very close together. Then, the outer coatings of the pronuclei disappear, and the male and female chromosomes mix to form a single nucleus.
... or the initiation of its development by any other means	Advances in cell biology have allowed embryonic development to be started by injecting a cell nucleus extracted from any cell in the body into an egg cell from which the nucleus has been removed (nuclear transfer). This is the basis of cloning technologies (see below). This part of the definition therefore means that once a cell is created (by nuclear transfer or any other means) that has the same potential to continue development as a cell formed by fertilisation of a human egg and a human sperm, it is included in the definition of a human embryo.
... not including any period when its development was suspended for any reason	Embryos created by IVF to achieve a pregnancy are often frozen at an early stage of development for later use. This part of the definition therefore means that the eight-week period when the developing organism is defined as an embryo does not include any time when it is frozen (or suspended by any other means).

[1]However, making a genetic change to a human embryo or to cells used to make an embryo (including eggs, sperm and their precursors), such as 'gene therapy' for treatment of genetic disorders, are banned practices under the *Prohibition of Human Cloning Act 2002*.

Stages of embryo development

In scientific terms, the early time period of development before the embryo becomes implanted in the uterus (approximately seven days) includes several stages:

Zygote	the single, fertilised cell before any division has occurred
Morula	a ball of about 30–60 undifferentiated cells inside an outer membrane
Blastula (or blastocyst)	a liquid-filled ball of about 100 cells with a single outer layer of cells (which form the placenta) and an inner mass of cells (which form the developing embryo and fetus)
Gastrula	stage of development when three embryonic germ layers (endoderm, ectoderm and mesoderm) are formed and aligned ready for growth and development of the organs and tissues.

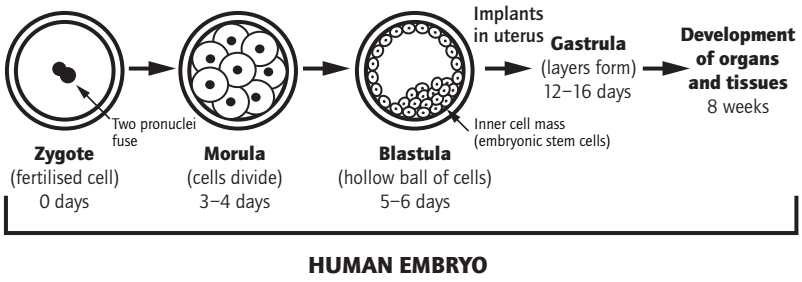

Figure 1 Stages in development of a human embryo

Thus, a human embryo is defined in the legislation as starting from the moment when the two pronuclei become visible (or development is initiated by other means) and as covering all stages of development to eight weeks. This definition of embryo does not distinguish the early stages of human development described above.

Human embryo clone

The terms ‘clone’ and ‘cloning’ have been used in the scientific literature to describe many types of genetic copying, from copies of sections of DNA (genes) to copies of plants (in agriculture) and cells cultured in a laboratory. The term first came to public prominence in connection with copying a whole animal, however, when the birth of Dolly the sheep was announced in 1997.

Neither of the Acts include a definition of ‘clone’, but the *Prohibition of Human Cloning Act 2002* includes a definition of ‘human embryo clone’.

Definition from legislation

A human embryo that is a genetic copy of another living or dead human, but does not include a human embryo created by the fertilisation of a human egg by a human sperm. [PHC Act, s 8(1)]

For the purposes of establishing that a human embryo clone is a genetic copy of a living or dead human:
(a) it is sufficient to establish that the set of genes in the nuclei of the cells of the living or dead human has been copied; and
(b) it is not necessary to establish that the copy is an identical genetic copy.
[PHC Act, s 8(2)]

For the purposes of the definition of a human embryo clone, a human embryo that results from the technological process known as embryo splitting is taken not to be created by a process of fertilisation of a human egg by a human sperm.
[PHC Act, s 8(4)]

What does it mean?

A human embryo ...	A human embryo clone is a type of human embryo (that is, unless otherwise stated, the term 'human embryo' includes human embryo clones).
... that is a genetic copy of another living or dead human	All cells in the body of a human are genetic copies of each other but, in human sexual reproduction, embryos are formed from a mixture of genetic material from the egg cell (mother) and sperm cell (father). This mixing is what makes each person unique. A human embryo created using the genetic material of only one person instead of two would be a genetic copy of that person.
... but does not include a human embryo created by the fertilisation of a human egg by a human sperm	This part of the definition is included so that identical twins and triplets (who are genetic copies of each other) are not included in the definition of a human clone. (See the discussion of embryo splitting below.)
For the purposes of ... (clarification of 'genetic copy')	This paragraph is included to clarify that 'genetic copy' does not mean an identical copy. This is because small amounts of genetic material remain in an egg cell even when the nucleus is removed (see below). There may also be small spontaneous differences in the genetic material between the cells of an individual or the DNA could be deliberately altered (see definition of 'human embryo', above).
For the purposes of ... (clarification of 'embryo splitting')	The second clarifying paragraph is included because it is possible to create a human embryo by IVF and, at the early cell division stages, artificially split it into two or more embryos, which are genetic copies of each other. The legislation says that any embryos made artificially this way are considered to be human embryo clones. However, when splitting occurs naturally (as for twins) this is not considered to be cloning (see above).

How could a human embryo clone be created?

A human embryo clone could be created by 'somatic cell nuclear transfer' (SCNT), a practice prohibited in Australia under the *Prohibition of Human Cloning Act 2002*. This method involves obtaining an egg cell from a woman in the same way eggs are obtained for IVF treatment. Using a very fine needle, the nucleus is extracted from the egg leaving only the cytoplasm. A nucleus is then extracted from a body (somatic) cell of a person (the same woman or another person) and inserted into the egg cytoplasm. Somatic cells are any cells in the body that are not eggs or sperm, or precursors of eggs or sperm. All the somatic cells of an individual are genetic copies of each other.

If the conditions are right, when the somatic cell nucleus is inserted into the egg cytoplasm, chemical factors in the cytoplasm stimulate the nucleus to divide in exactly the same way that a naturally created embryonic nucleus would do after the egg and sperm have fused. In other words, an embryo is formed in which all the genetic material has come from one person (the donor of the somatic cell nucleus) instead of from two people, as would be the case for natural fertilisation.

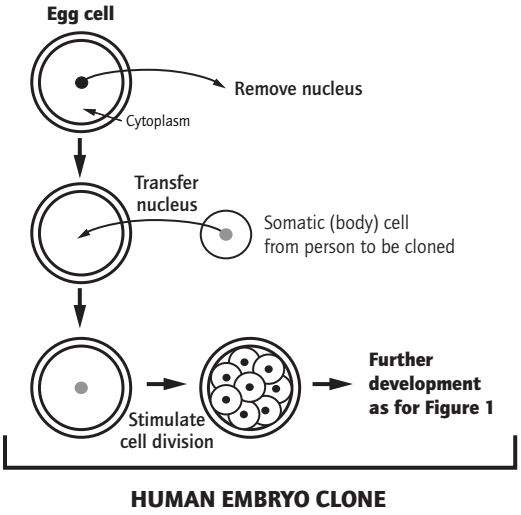

Figure 2 Creation of a human embryo clone by somatic cell nuclear transfer

Other methods of creating embryo clones include splitting an embryo at the early cell division stage or inserting an embryonic stem cell nucleus into egg cytoplasm. In some mammals (for example, mice and primates), egg cells have been stimulated to become embryos without fertilisation by sperm (a process called parthenogenesis), although such embryos have not been viable. Creation of a human embryo using any of these procedures is prohibited in Australia.

What could a human embryo clone be used for?

Both in the scientific literature and in media reporting of human cloning, two types of human cloning have been distinguished:

- Reproductive cloning — when the intention is to implant a human embryo clone into a woman to achieve a pregnancy.
- Nonreproductive cloning (also known as 'therapeutic' cloning) — when a human embryo clone is created and then destroyed after a few days to obtain embryonic stem cells that are compatible with the person of whom the human embryo clone is a genetic copy (see section below on 'What is special about stem cells from human embryo clones?').

'Nonreproductive cloning', 'cloning for research purposes' and 'nuclear transfer' are alternative terms for 'therapeutic cloning' but these terms are not widely used.

Stem cells

What are they?

Stem cells are unspecialised 'parent' cells that can replicate themselves and have the potential to differentiate into specialised cell and tissue types. Stem cells occur at all stages of human development, from embryo to adult, but their versatility and abundance decrease with age.

In adults, most tissues and organs have some stem cells. For example, skin has stem cells in the lower layers that generate new skin as old skin is lost; similar cells in the gut regenerate the lining of the intestines; cells in bone marrow generate new blood cells as old ones are lost; and so on. These cells are called 'adult stem cells'. Some adult stem cells (such as some of those in bone marrow) can produce several different cell types. These are called *multipotent stem cells*.

At the very early stages of embryo development, each cell can, if separated, develop into a whole organism. This is the basis of embryo splitting (see above) and such cells are called *totipotent stem cells*. At the blastula stage, the cells start to become more specialised and, from this stage onwards, each cell cannot develop into a whole organism. Nevertheless, the cells in the centre of the blastula are very versatile and can turn into almost any type of cell in the body. Cells with this potential are called *pluripotent stem cells*. Inner cell mass cells isolated from a blastula and cultured for use in stem cell research are referred to as 'embryonic stem cells'.

Stem cells also occur at later stages in embryonic development (when they are called 'embryonic germ cells'), in fetuses and in blood from the umbilical cord of a newborn baby.

There is continuing controversy among researchers about some aspects of stem cell classification and terminology. Uncertainties include whether some cells regarded as multipotent are, in fact, pluripotent; the capacity of some stem cells that are committed to one developmental pathway to be redirected along another (a concept that has been called 'plasticity'); and the relative potentials of adult and embryonic stem cells.

Why are scientists interested in stem cells?

Stem cells are of great interest to researchers because of their potential to regenerate damaged or diseased tissues. The treatment of leukaemia patients with bone marrow containing blood stem cells from compatible donors has been a routine procedure since the 1970s. Since that time, scientists have hoped to develop other stem cell therapies. Stem cells also provide a good model for research on the development and function of different cell types and the features of certain cellular disease states. Embryonic stem cells have attracted particular interest because they are pluripotent (see above).

Stem cells from human embryo clones have attracted additional interest because they provide an opportunity to obtain embryonic stem cells that are a precise match for the person of whom the human embryo clone is a copy. Treatment of this person with their own matched stem cells would prevent immune rejection problems and/or avoid having to wait for a suitable matched donor. The same would be true of adult stem cells if they were obtained from a person requiring stem cell treatment.

Assisted reproductive technology

The *Research Involving Human Embryos Act 2002* refers to the operation of ART centres, and to 'excess ART embryos' (see Section 5 of this Issues Paper). ART is defined in the National Health and Medical Research Council *Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research* (2004) as:

> The application of laboratory or clinical techniques to gametes and/or embryos for the purposes of reproduction.

This covers IVF and other related procedures to create embryos in a laboratory for implantation into a woman to achieve a pregnancy, plus any associated manipulations of the gametes (eggs or sperm) or embryos (including for diagnostic procedures, such as genetic screening). It also covers all clinical procedures involving donated and artificially inseminated sperm or donated eggs.

Other definitions

Other important terms from the legislation are defined in Sections 4 and 5 of this Issues Paper.

Issues — definitions and terminology

As with all legal documents, the two Acts rely on legal definitions and terminology. Scientific definitions and community understanding, on the other hand, are evolving. Public discussion and review of the Acts requires a common understanding of the terminology used. The Committee would therefore like to hear the views of the Australian community on any aspect of the definitions and terminology used in the Acts. In particular:

- **Are the definitions of 'human embryo' and 'human embryo clone' clear and unambiguous? Do they appropriately reflect community standards? Do they cover all of the activities that should be regulated under the legislation?**
- **Are other definitions and terminology used in the Acts helpful for understanding and interpreting the legislation? Do they appropriately reflect community standards?**
- **Does the legislation need to define stem cells? Is the focus on the use of excess ART embryos sufficient?**

The Committee would also like to hear the views of researchers, ART providers and people who use ART services on the following questions:

- **Have there been any problems in interpreting or applying any of the definitions or terminology in the Acts in research or ART practice?**
- **Do you foresee any such problems arising (for example, because of new scientific advances, changing scientific understanding of biological processes, or changes in ART practice)?**

The Committee would also like to hear the views of government on the following question:

- **Have there been any problems in interpreting or applying the definitions and terminology used in the Acts?**

Note: These questions relate to definitions and terminology only. Further discussion of the scope of the legislation is in Sections 4 and 5 of this Issues Paper.

4 *Prohibition of Human Cloning Act 2002*

Note for readers: Sections 4 and 5 of this Issues Paper provide summaries of the most important sections of the legislation, with some simple explanations of key concepts. However, **for full details, readers should look at the original legislation and the Explanatory Memoranda** (see 'References and further reading' with this Issues Paper, or the Legislation Review website, http://www.lockhartreview.com.au). Although some specific issues are highlighted in this paper, the Committee would like to receive comments on any aspect of the scope or operation of the legislation.

Object of the Act

> The object of the Act is to address concerns, including ethical concerns, about scientific developments in relation to human reproduction and the utilisation of human embryos by prohibiting certain practices. [PHC Act, s 3]

Prohibited embryos and practices

The *Prohibition of Human Cloning Act 2002* prohibits the creation, placing in the human body or the body of an animal, import or export of a human embryo clone, whether or not it did not or could not have survived.

The Act also prohibits a number of other practices as follows:

- Creating a human embryo by a process other than by fertilisation of a human egg by a human sperm, or intentionally developing such an embryo.
- Creating a human embryo outside the body of a woman for any purpose apart from attempting to achieve a pregnancy.
- Creating or developing any of the following embryos:
  - a human embryo with genetic material from more than two people
  - a human embryo created using precursor cells from a human embryo or fetus
  - a human embryo in which the genome has been altered in any way that could be inherited by the descendants of the embryo
  - a chimeric or hybrid embryo.
- Developing a human embryo outside the body of a woman for more than 14 days, excluding any period when development is suspended.
- Collecting a viable human embryo from the body of a woman.

Embryos created or obtained using any of the above practices are collectively referred to in the Act as 'prohibited embryos'. Import and export of prohibited embryos are banned, as is placing such embryos into the body of a woman.

The following practices are also prohibited:

- Placing a human embryo in the body of an animal or an animal embryo in the body of a human.
- Placing a human embryo in the body of a human except in a woman's reproductive tract.
- Commercial trading in human eggs, sperm or embryos (not including the payment of reasonable expenses in connection with the supply).

Explanation

The combined prohibition of 'human embryo clone' and 'human embryo created other than by fertilisation of a human sperm and human egg' was made deliberately broad to include any emerging techniques that could be used to create human embryos.

The ban on creating a human embryo with genetic material from more than two people avoids confusion of genetic identity for the person born. This prohibition prevents procedures such as adding additional cytoplasm from a donor egg (or other cell) to the patient's egg to boost the chance of successful fertilisation, because this would introduce small amounts of genetic material from the donated cytoplasm (contained in specialised cellular components called mitochondria).

The ban on using precursor cells prevents creation of a human embryo using cells that are the precursor cells for sperm or eggs obtained from another human embryo or from a fetus (due to concerns that it may be possible to create a human who has never had a living genetic parent).

The ban on creating a human embryo with an altered genome prevents genetic manipulation of eggs, sperm or embryos to overcome a genetic illness or disorder (or to enhance physical characteristics). Preimplantation genetic diagnosis does not fall into this category because, in this case, embryos are selected based on their existing genetic make-up with no additional genetic manipulation.

The ban on chimeric and hybrid embryos prevents:

- introduction of any animal cells (or cell components) into a human embryo (chimeric embryo)
- creation of embryos by fertilisation of any combination of animal and human eggs and sperm, or by nuclear transfer between animal and human cells (hybrid embryos).

The ban on developing a human embryo outside the body prevents any attempts at creating a fetus or baby outside the body of a woman. Limiting the time allowed to 14 days aligns the legislation with the National Health and Medical Research Council *Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research* (2004) and the Reproductive Technology Accreditation Committee *Code of Practice for Centres Using Reproductive Technology* (2002). The time limit excludes any time when development is suspended (such as when the embryo is frozen). ART embryos are usually implanted at between three and seven days of development.

The ban on collecting a viable embryo from the body of a woman prevents a procedure called 'embryo flushing', which is the removal of a viable embryo from the uterus — a technique commonly used in animal husbandry but not, to date, in humans.

The bans on placement prevent development of a human embryo in any environment other than a woman's uterus. Placing an animal embryo into a human or vice versa is also banned.

The ban on commercial trading of gametes (eggs and sperm) and embryos is to prevent the 'commodification' of human life and includes any payment in cash or kind ('valuable consideration', including inducements, discounts and priority services), but not reimbursement of reasonable expenses of a donor (such as travel and accommodation).

Further information on the import and export of human embryos is included in Section 6 of this Issues Paper.

14

Offences

Under the *Prohibition of Human Cloning Act 2002*, creating, developing, placing, importing or exporting of a human embryo clone carries a maximum penalty of 15 years in prison. Other offences carry a maximum penalty of 10 years in prison. Since the introduction of the legislation, no prosecutions have been made. (See Section 5 of this Issues Paper for information about monitoring and compliance arrangements.)

Issues — prohibited embryos and practices

One of the effects of these prohibitions has been to specifically ban the creation of a human embryo clone by somatic cell nuclear transfer (or by any other means) for use in research. This means that researchers in Australia have not been allowed to research and develop methods to create human embryo clones and extract matched human stem cells for research on cellular therapies (see Section 3 of this Issues Paper). This issue is the subject of considerable debate around the world, with some countries allowing the creation of human embryo clones for use in research, and some (like Australia) not allowing it (see Section 8 of this Issues Paper).

The debate is polarised — some of the main arguments are shown below:

- ***Against:*** **As a human embryo clone is a human embryo (capable of becoming a human being), it is wrong to create one specifically to destroy it. Adult stem cells show similar potential for development of stem cell therapies as embryonic stem cells and their use does not involve the destruction of human embryos.**
- ***For:*** **It is acceptable to create and use preimplantation human embryos for research that may benefit human health and wellbeing by development of stem cell therapies to repair damaged and diseased tissues. It is not known at this stage whether embryonic or adult stem cell research will provide greater benefits (if any), so it is legitimate to progress both pathways until a clearer picture emerges.**

The Committee would like to hear the view of researchers, consumer groups representing recipients of potential therapies, and others, about these issues. In particular:

- **How has the ban on all human cloning affected research in Australia?**
- **How have the other prohibitions affected research in Australia?**

The Committee would also like to hear from governments, special interest and community groups (including religious groups), and others, about the overall scope of the prohibitions. In particular:

- **Are the prohibited embryos and practices described in the Act still relevant in light of advances in biotechnology since 2002? Do they appropriately reflect community standards?**
- **Has the prohibition of payment beyond reasonable expenses (valuable consideration) for gametes and embryos affected access to these items?**

See also Section 7 of this Issues Paper for an invitation to tell the Committee more about the current research position and potential benefits of future research.

5 *Research Involving Human Embryos Act 2002*

Object of the Act

> The object of the Act is to address concerns, including ethical concerns, about scientific developments in relation to human reproduction and the utilisation of human embryos by regulating activities that involve the use of certain human embryos created by ART. [RIHE Act, s 3]

Use of excess ART embryos

The *Research Involving Human Embryos Act 2002* lays down conditions for the use of human embryos that have been created by assisted reproductive technology (ART) to help couples become pregnant. The Act distinguishes between ART embryos that form part of an ongoing treatment program and 'excess ART embryos'.

An excess ART embryo is defined as a human embryo that was created by ART for use by a woman to become pregnant but is no longer required for this purpose. An embryo can only be considered to be an excess ART embryo if there is a written authority to this effect signed by both:

- the woman for whom the embryo was created
- her spouse (if any) at the time the embryo was created.

Building on this definition, the legislation has three main provisions:

- Use of a human embryo that is not an excess ART embryo is **prohibited** for any purpose other than for the ART treatment of a woman to achieve a pregnancy and carried out by an accredited ART centre.
- Use of an excess ART embryo, including research, is **allowed** if authorised by a licence from the Embryo Research Licensing Committee of the NHMRC (see below). These activities require 'proper consent' from all 'responsible persons'.
- Use of an excess ART embryo is **allowed** without a licence for certain 'exempt uses'. Such activities require consent in accordance with arrangements for the clinical practice of ART.

Explanation

'Spouse' is defined as anyone living with a person as their partner on a bona fide domestic basis.

An 'accredited ART centre' is either a person or organisation accredited by the Reproductive Technology Accreditation Committee (RTAC) against the *Code of Practice for Assisted Reproductive Technology Units* (RTAC 2005), which is developed by the profession for the accreditation of ART centres in Australia. Such centres, as well as public and privately funded research involving ART, are also expected to comply with National Health and Medical Research Council ethical guidelines.

'Exempt uses' are storage, removal from storage, transport, observation, allowing embryo to succumb, donation to another woman to achieve a pregnancy. In cases where the embryo is biologically unfit for implantation, exempt uses also include diagnostic investigations by an

ART centre that directly benefit the woman for whom the embryo was created in future attempts at conception. All other activities or projects (such as research, training or quality assurance activities) require a licence.

'Proper consent' is defined as consent obtained in accordance with the NHMRC ethical guidelines on ART (see 'Regulations' below). The current edition of these guidelines (2004) states that the clinical decision to declare an embryo as an excess ART embryo must be made before, and separately from, consent for a specific use of the embryo (such as for research).

'Responsible persons' are defined as:

- each person who provided the egg or sperm from which the embryo was created and their spouses (if any) at that time; and
- the woman for whom the embryo was created to achieve a pregnancy and her spouse (if any) at that time.

The legislation does not regulate the use of embryonic stem cells once they have been derived, under licence, from an excess ART embryo. Guidance on this matter is provided by the NHMRC Australian Health Ethics Committee and overseen by institutional human research ethics committees (HREC). Research on adult and fetal stem cells is not affected by the legislation. For further information on stem cells, see Section 3 of this Issues Paper.

Issues — use of excess ART embryos

Unless an embryo has been declared an excess ART embryo by the woman or couple for whom it was created, it can only be used for attempting to achieve a pregnancy in the woman. With the exception of some exempt uses, before an embryo can be used for any other purpose, a licence must be obtained from the Licensing Committee and consent obtained from those responsible for the embryo.

The Committee would like to hear about the scope and operation of these arrangements from ART providers, consumers of ART services, special interest and community groups (including religious groups), government regulatory personnel, and others. In particular:

- **Are the provisions of the legislation with respect to the use of excess ART embryos clear and unambiguous? Do they appropriately reflect community standards?**
- **Have any issues arisen with respect to the operation of the legislation (such as with giving and obtaining consent for an embryo to be an excess ART embryo; or giving and obtaining consent from responsible persons for the use of excess ART embryos in research)?**
- **Are the arrangements for accreditation and ethical oversight of ART centres appropriate?**

Licensing and statutory arrangements

Establishment of the Embryo Research Licensing Committee

The Act sets out a regulatory framework for the Embryo Research Licensing Committee as a principal committee of the NHMRC (referred to in this paper as the 'Licensing Committee'). The nine members of the Licensing Committee are appointed by the Australian minister with portfolio responsibility for human cloning and embryo research, in consultation with the States and Territories. The functions of the committee are to:

- consider applications for licences to conduct research on excess ART embryos
- grant licences in conformity with the Act
- regularly (at least every six months) report to the Australian Parliament
- maintain a public database of licences granted with name of licence holder, short statement of project, any conditions, number of excess ART embryos authorised, date and period of licence
- appoint inspectors for monitoring and compliance (the Act also establishes the obligations and monitoring powers of inspectors).

Confidential commercial information must not be disclosed by Licensing Committee members (or others who have access to it) to anyone except those involved in the functions of the Act.

Licensing system

The Licensing Committee must not issue a licence unless it is satisfied that the following conditions are met:

- The proposal includes a protocol for obtaining proper consent for the proposed use of excess ART embryos from all responsible persons (see above), and for managing any restrictions on the consent.
- The activity or project has been assessed by an HREC following guidelines set out in the NHMRC National Statement (see 'Regulations' below). The assessment must be available for consideration by the Licensing Committee.

The Licensing Committee must also consider:

- whether the number of ART embryos is restricted to that likely to be necessary to achieve the goals of the activity or project
- the likelihood of the proposed project achieving a significant advance in knowledge or improvement in technologies for treatment, which could not reasonably be achieved by other means
- any relevant NHMRC guidelines (see 'Regulations' below)
- the HREC assessment of the application.

Initially, the use of excess ART embryos in research that may damage or destroy the embryo was restricted to those embryos created before 5 April 2002. This restriction lapsed on 5 April 2005. Licensed researchers may now use excess ART embryos created since 5 April 2002. However, the criteria for obtaining a licence, and for monitoring compliance remain.

The Licensing Committee must notify its decision, including any conditions, to the applicant, the HREC and the relevant State or Territory. The committee can suspend or revoke a licence if it believes that the conditions of the licence have been breached. Applicants can appeal a decision to the Administrative Appeals Tribunal.

Licences granted

Since the establishment of the Licensing Committee, nine licences have been granted; four for obtaining embryonic stem cells, four for improvements in ART, and one for training embryologists.

Some applications have required revision to meet Licensing Committee requirements; none have been rejected. Together, the nine current licences authorise the use of up to 1740 excess human embryos.

Monitoring and compliance

Inspectors are responsible for monitoring compliance with both the *Research Involving Human Embryos Act 2002* and the *Prohibition of Human Cloning Act 2002*. They report to the chairperson of the Licensing Committee.

Monitoring and compliance activities cover organisations licensed under the *Research Involving Human Embryos Act 2002* and organisations that do not hold a licence but are undertaking activities relevant to the legislation. Inspectors are authorised to enter any premises if the occupier is undertaking activities authorised by a licence and it is at a reasonable time.

Inspectors have established arrangements with the Australian Federal Police and relevant State and Territory agencies. These ensure the exchange of information, and cooperation in relation to monitoring activities and investigations of suspected breaches of both the Australian Government and corresponding State and Territory legislation.

Regulations

The Research Involving Human Embryos Regulations 2003 prescribes the guidelines that the Licensing Committee must take account of in issuing and overseeing a licence. These are:

- *Ethical Guidelines on Assisted Reproductive Technology*, issued by the NHMRC in 1996
- *National Statement on Ethical Conduct in Research Involving Humans*, issued by the NHMRC in 1999 (National Statement).

However, the former of these guidelines has been updated and replaced by:

- *Ethical Guidelines on the Use of Assisted Reproductive Technology in Clinical Practice and Research*, issued by the NHMRC in 2004.

The amendment to the Regulations to take account of this change will come into force in about September 2005.

The Regulations also include the list of organisations from which members of the Licensing Committee can be appointed.

Offences

Offences under the *Research Involving Human Embryos Act 2002* carry a maximum penalty of five years in prison. Since the introduction of the legislation, no prosecutions have been made.

Issues — licensing and statutory arrangements

The Committee would like hear about the operation of the licensing system from all those involved in licensing arrangements, including government regulatory personnel (Australian, State, Territory), the Licensing Committee, researchers who have applied for a licence, human research ethics committees, ART providers, users of ART services, and others. In particular:

- **Have researchers or ART providers experienced any uncertainty about when to apply for a licence?**
- **Have there been any difficulties of interpretation or application of the criteria for granting a licence?**
- **Are the monitoring and compliance requirements of the Act appropriate?**
- **Are there any other issues relating to the operation of the licensing system?**

6 International exchange of embryos and stem cells

Controversy around international exchange of embryos and stem cells is related to ethical concerns about the sources of these materials. The current legislation is designed to ensure that stem cell lines cannot be used in Australia if they were derived overseas using practices that are prohibited in Australia. These issues are specifically included in the terms of reference for the Legislation Review (see Appendix 2 of this Issues Paper) and the Committee welcomes submissions on any relevant matters.

Import and export of embryos

The *Prohibition of Human Cloning Act 2002* makes it an offence to import, export or place in the body of woman a 'prohibited embryo' (that is, one that is not permitted to be used in Australia; see Section 4 of this Issues Paper).

In February 2003, the Customs (Prohibited Exports) Regulations 1956 were amended to prohibit the export of human embryos. However, in March 2003, further amendments were made to the Regulations to allow the Minister for Customs to consider an application for export of a human embryo for the sole purpose of implantation in the prospective mother or a relevant woman (as described in the Regulations) to achieve her pregnancy. An application may only be made by the prospective mother or, in the event that the prospective mother has died, the spouse of the prospective mother at the time that the embryo was created or donated. These arrangements are in place until July 2006, and are currently being reviewed as part of this Legislation Review.

The Australian Quarantine and Inspection Service administers quarantine arrangements for the import of human embryos, sperm and eggs. These items can be imported for human therapeutic use (including implantation), artificial insemination or IVF.

Other countries also regulate the import and export of reproductive materials. For example, both Canada and the United Kingdom require a licence from their regulatory authority. However, stem cell lines, once developed, are not reproductive materials and therefore not covered by these arrangements.

Trading in human embryos (and human sperm and eggs) is prohibited in Australia under the *Prohibition of Human Cloning Act 2002* (see Section 4 of this Issues Paper).

Import and export of stem cells

In Australia, the Customs (Prohibited Imports) Regulations 1958 were amended in February 2003 to prohibit the import of viable materials derived from human embryo clones because they are a byproduct of a process (human cloning) that is outlawed in Australia. The Customs (Prohibited Exports) Regulations (see above) prohibit the export of human fluids, cells and tissues if the internal volume of the immediate container in which the material is packed exceeds 50 millilitres. This provision means that most cell lines can be legally exported as the vials are well under the volume limit.

Interim advice from the Australian Health Ethics Committee (currently under review) has recommended that research proposals involving the use of embryonic stem cells should be reviewed by an institutional human research ethics committee (HREC). If the HREC is not sure that the cell line was derived in accordance with standards operating in Australia, then the research should not be approved. These considerations do not apply to adult stem cells.

Internationally, it is difficult to know exactly how much trade in stem cells and stem cell lines occurs, with some exchange happening informally between scientists and research organisations. In some countries, funding decisions provide the means to ensure the use of only embryonic stem cells lines derived within required ethical standards. In the United States, federal funding for stem cell research is only available for those laboratories that use a specified range of stem cell lines, all derived from excess ART embryos created before 9 August 2001. In Europe, European Union funding was initially linked to embryonic stem cells derived before a particular date. This position later shifted to funding stem cell research, but prohibiting funding of research to create embryos for the purpose of obtaining stem cells.

Issues — international exchanges of embryos and stem cell lines

The Committee would like to hear from ART providers, users of ART services, government regulators, and others, about import and export of embryos and stem cell lines. In particular:

- **How have the import and export prohibitions (including the amendments to the Customs Regulations) affected the operation of ART centres, the access to reproductive materials by users of ART, or donation of reproductive materials by donors?**
- **How has the legislation (including the Customs Regulations) affected stem cell research activities?**

Stem cell registries and banks

Regulatory requirements (knowing the source of embryonic stem cells, and being able to ensure the safety of any subsequent therapeutic uses) and the desire of research organisations to collaborate to share resources and data, are driving the development of stem cell registries and banks.

Registries hold a record of stem cell lines (for adult, fetal and embryonic stem cells), enabling researchers to track down suitable stem cell lines for their work. Examples include:

- the United States National Institutes of Health Human Embryonic Stem Cell Registry, which lists the derivations of stem cells eligible for federal funding with contact information to help researchers access the cell lines
- a registry maintained by the International Society for Stem Cell Research, which publishes data on cell lines not eligible for United States federal funding, available from both public and private agencies.

There are plans for other registries, including a European stem cell database and stem cell registry, and a Canadian registry of embryonic stem cell lines generated in Canada.

Stem cell banks hold actual cell lines. Cell banks have existed for other types of cultured cells but the first cell bank specific for stem cells was opened in 2004. The UK Stem Cell Bank is funded by the United Kingdom Government and managed by the National Institute for Biological Standards and Control. It aims to bank or store quality-controlled and well-characterised adult, fetal and embryonic stem cell lines for both basic and clinical research in the United Kingdom and internationally, and also to deliver banks of stem cells for use in the production of therapeutic materials. The bank will be open to publicly and privately funded researchers from the United Kingdom and overseas. It will also provide information on the cell lines in the bank and the technology used in their preparation and

characterisation. There are also plans for stem cell banks in the United States, South Korea and China.

One of the statutory requirements for these reviews of the Australian legislation is to consider 'the applicability of establishing a National Stem Cell Bank' (see Appendix 2 of this Issues Paper).

Issues — national stem cell bank

The Committee would like to hear from researchers and others with an interest in stem cell issues, about the applicability of setting up a national stem cell bank in Australia. In particular:

- **Who would use a national stem cell bank in Australia?**
- **What would be the advantages of an Australian stem cell bank?**
- **How should an Australian stem cell bank be administered?**
- **How should the community be involved in such as stem cell bank?**
- **Do Australian researchers have appropriate access to stem cell banks in other countries (such as the UK Stem Cell Bank)?**

7 Research developments

The terms of reference for the Legislation Review require the Committee to take account of:

- developments in technology in relation to assisted reproductive technology (ART)
- developments in medical and scientific research, and the potential therapeutic applications of such research (see Appendix 2 of this Issues Paper).

Since 2002, medical and scientific research has continued at a rapid rate. Some areas of particular focus are:

- developments in human embryology — research to support ART treatment of infertile couples
- developments in stem cell science and cellular therapies
  - basic stem cell science
  - cell therapy research (animal studies and some clinical trials).

Issues — research developments

The Committee would like to hear from ART researchers, users of ART services, and others, about developments in human embryology. In particular:

- **Has the access to excess ART embryos for research allowed a significant advance in knowledge and technology in ART?**
- **What are the next steps in the research? What are the potential benefits of the research? What are the potential risks?**

The Committee would like to hear from stem cell science and cellular therapy researchers, consumer groups representing potential recipients of stem cell therapies, and others, about developments in these areas. In particular:

- **Have the advances in stem cell research been greater or less than expectations in 2002?**
- **Has the access to excess ART embryos for research allowed a significant advance in knowledge in this area?**
- **What are the next steps in the research? What are the potential benefits of the research and when might these occur? What are the potential risks?**

8 Legislation in other countries

There is a spread of legislative and regulatory responses across different countries, reflecting variations in historical and cultural heritage. No country specifically allows human reproductive cloning in their legislation.

In countries were there is legislation or regulations on human cloning, three broad approaches have been taken:

- Prohibit reproductive cloning but do not specifically prohibit nonreproductive cloning. This is the position in New Zealand, Greece and South Korea.
- Prohibit both reproductive cloning and nonreproductive cloning. This is the position in Australia, Canada and several European countries.
- Prohibit reproductive cloning but specifically allow (under licence) nonreproductive cloning. This is the position in the United Kingdom, Belgium and China.

There is also considerable variation between countries on other aspects of research on human embryos, including:

- whether excess ART embryos can be used in research — some countries permit this (for example, Australia, Canada, United Kingdom and Singapore); others prohibit all such research (for example, Italy)
- whether human embryos can be specifically created for the purpose of research or to develop therapeutic applications — this could be done by the union of an egg and sperm, or by cloning (United Kingdom, Belgium, Sweden, China, South Korea, Singapore all permit this).

In March 2005, agreement was reached at the United Nations for a nonbinding resolution to ‘prohibit all forms of human cloning inasmuch as they are incompatible with human dignity and the protection of human life’. However, 35 countries did not support the resolution, arguing that cloning for research purposes (therapeutic cloning) should be distinguished from reproductive cloning, and permitted.

Appendix 1 Legislation Review Committee

The Hon John S Lockhart AO QC (Chair)

The Honourable John Lockhart is a highly regarded member of the international legal community. He was a Justice of the Federal Court of Australia from 1978 until 1999. He has been a member of the Appellate Body of the World Trade Organization, Geneva, Switzerland since 2002 and was appointed as the Deputy Chair of the International Legal Services Advisory Council in 1994. Mr Lockhart has highly relevant experience in chairing high-level committees that deliberate on contentious issues.

Professor Peter Schofield (NSW)

Professor Schofield is a renowned neuroscientist. He is Executive Director and Chief Executive Officer of the Prince of Wales Medical Research Institute, Senior Principal Research Fellow at the Garvan Institute of Medical Research and Conjoint Professor at the Faculty of Science and Faculty of Medicine at the University of New South Wales. Professor Schofield's skills and expertise are in a highly relevant scientific discipline to the review subject matter.

Associate Professor Ian Kerridge (NSW)

Professor Kerridge is a highly regarded clinical ethicist and specialist haematologist. He is Associate Professor in Bioethics and the Director of the Centre for Value, Ethics and the Law in Medicine at the University of Sydney and staff haematologist/bone marrow transplant physician at Westmead Hospital, Sydney. Professor Kerridge has highly relevant skills and expertise demonstrated through his work and publications in the field of health ethics.

Professor Loane Skene (Vic)

Professor Skene is a renowned lawyer, ethicist and academic. She is Pro Vice-Chancellor, Professor of Law in the Law Faculty and an Adjunct Professor of Law in the Faculty of Medicine, Dentistry and Health Sciences at the University of Melbourne. Professor Skene has highly relevant skills and expertise demonstrated through her work and publications in the fields of health law and ethics.

Professor Barry Marshall (WA)

Professor Marshall is a highly awarded scientist of international renown who is also a successful community advocate both in Australia and overseas. He is a specialist gastroenterologist, noted for his discovery of the link between the bacteria *Helicobactor pylori* and gastric ulcers. He is Research Professor of Microbiology at the University of Western Australia and also brings generalist scientific expertise in addition to his abilities in community representation.

Associate Professor Pamela McCombe (QLD)

Associate Professor McCombe is a Consultant Neurologist and a Visiting Medical Officer at the Royal Brisbane Hospital and holds the position of Associate Professor, Department of Medicine at The University of Queensland. She is Chair of the Wesley Research Institute Research Committee and Chair of the Scientific Program Committee of the Australian Association of Neurologists.

Appendix 2 Legislation Review Committee terms of reference

1. The Legislation Review Committee — *Prohibition of Human Cloning Act 2002* and the *Research Involving Human Embryos Act 2002* is required to consider and report on the scope and operation of each of the *Prohibition of Human Cloning Act 2002* and the *Research Involving Human Embryos Act 2002* taking into account:

   (i) the following statutory requirements:

   a) developments in technology in relation to assisted reproductive technology;

   b) developments in medical research and scientific research and the potential therapeutic applications of such research;

   c) community standards;

   d) the applicability of establishing a National Stem Cell Bank; and

   (ii) the following additional matters in relation to the national legislative scheme:

   a) consideration of relevant aspects of State and Territory legislation corresponding to the *Research Involving Human Embryos Act 2002*;

   b) the role played by State and Territory statutory bodies that regulate assisted reproductive technology (ART) treatment as well as the role of national organisations including, but not necessarily limited to, the Fertility Society of Australia and its Reproductive Technology Accreditation Committee (RTAC);

   c) the effectiveness of monitoring and compliance under the *Research Involving Human Embryos Act 2002* in particular, but also in relation to the *Prohibition of Human Cloning Act 2002* to the extent that issues may arise in relation to the latter Act;

   d) the ongoing appropriateness and effectiveness of changes to the Customs regulations to regulate the export of human embryos derived through ART and the import of viable materials derived from human embryo clones;

   e) options for regulation of the import and export of human embryonic stem cells;

   f) the implications of cost recovery; and

   g) implications for Australian science and economic activity.

2. The Legislation Review Committee is required to consult the Commonwealth, the States, the Australian Capital Territory and the Northern Territory and a broad range of persons with expertise in or experience of relevant disciplines.

3. The reports must, to the extent that it is reasonably practicable, set out the views of the Commonwealth, the States and Territories and those other persons consulted.

4. Each report must contain recommendations about amendments, if any, that should be made to the *Prohibition of Human Cloning Act 2002* and the *Research Involving Human Embryos Act 2002*, whichever is applicable.

5. The Legislation Review Committee is required to give a written report to the Council of Australian Governments and both Houses of the Parliament on the independent review of the operation of the *Prohibition of Human Cloning Act 2002* no later than Monday 19 December 2005. The Legislation Review Committee is required to give a written report to the Council of Australian Governments and both Houses of the Parliament on the independent review of the operation of the *Research Involving Human Embryos Act 2002* as an accompanying report to the report on the review of the operation of the *Prohibition of Human Cloning Act 2002*.

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State and Territory government legislation

http://www.nhmrc.gov.au/embryos/information/legislation/index.htm

Appendix 3 List of submissions

Submission	Individual/Organisation
1	Damian Pierre Ziegelaar
2	Bert Van Galen
3	Dr Jim Cummins
4	Confidential
5	Gary Cartmer
6	Dr Vaughan Davis
7	E Hinton
8	Marie Everett
9	Graham Sievers
10	Georgina Bain
11	Gerald Gibson
12	Shirley Fallon
13	M Usher
14	Mary O'Hanlan
15	Eileen Hogg
16	Confidential
17	Coalition For The Advancement of Medical Research in Australia (CAMRA)
18	Australian Academy of Science
19	Marjorie Crowley
20	Jo George
21	Jim and Julie-Ann McLoughlin
22	Adele and Jeffrey Greenaway
23	Phyllis Doheny
24	Peter Dolan
25	Denis Symon
26	Michael Siddle
27	Graham & Joanne Russell
28	Charles Fivaz
29	Leone Carse
30	Mark McMahon
31	Ellen Stack
32	Patricia Barwell
33	Eric McKinnon
34	Mary Sehir
35	Bernadette Lawcett

Submission	Individual/Organisation
36	JM Buchanan
37	Sister M Martin
38	Marie Carey
39	MF De Carvalho
40	JS & M Scrogings
41	Claire Lennon
42	M Woodrow
43	Kathleen Hetherington
44	CE Geary
45	Joseph Holloway
46	Allan and Marie Kennedy
47	Farther Max Barrett
48	Gerald Shiel
49	James Joyce
50	Manfred Schlesier
51	N Chowne
52	Patricia Carty
53	Janice Goodwin
54	Winifred Klomp
55	Thelma Joyce
56	Joy Hockings
57	Grahame Hobbs
58	Neil Ryan
59	John McGovern
60	Eileen Talbot
61	JV Dolahenty
62	Marie Clarke
63	Margaret Mifsud
64	Jennie Wilson
65	John Lovell
66	John Lennon
67	Hannah Jekki
68	Elizabeth Connolly
69	Jean Pinch
70	K O'Brien
71	Margaret Wilson
72	Veronica Altham
73	PT Flanigan

Submission	Individual/Organisation
74	Matilda Felice
75	R Langusch
76	Sister Elizabeth Hayes
77	Val O'Brien
78	Stephen Kucharik
79	Steve & Kim Instance
80	Margaret Instance
81	Frances Kirby
82	Nanango Christian Faith Centre Inc
83	Annabelle Atayde
84	Mark Lynch
85	Catherine Llewellyn-Smith
86	Clara Carboni
87	Ann Clementine
88	Rose Shortt
89	Janet O'Reilly
90	Sister GP Lindner
91	Confidential
92	John Moran
93	Confidential
94	Mark and Elena Reidy
95	Aileen Knight
96	Sheelagh Abela
97	George and Maureen Wright
98	June Menzies
99	OM Dempsey
100	AG O'Neill
101	B O'Neill
102	Lilah Monk
103	Gerard Dick
104	Professor Barry Rolfe
105	Confidential
106	L & I Voesenek
107	Patricia Landrigan
108	B McGinnity
109	David Beke
110	Andrew and Judith Beke
111	Sister Mary Cummins
112	Emma Kramer
113	Maxine White
114	Laura Bentley
115	Veronica Measki
116	Lucy Blundell
117	M Baker
118	Audrey English
119	Sister M Cooke
120	O'Connor Catholic Women's League
121	Confidential
122	Reese Powell
123	Leslie Sullivan
124	CJ Cotter
125	J Murphy
126	J Poynting
127	Cathy Smith
128	E Laws
129	Karen Rooke
130	Y Graham
131	Maureen Federico
132	Alice Fiumara
133	Coral Whipper
134	EV Corry
135	Jenny Spinks
136	Estelle Clancy
137	Douglas and Shirly McCray
138	Helena Knox
139	Bernadette Curtis
140	M Weeks
141	C Dowse
142	Robert Murphy
143	Anne Oldroyd
144	A Caravello
145	Andrea Calilhanna
146	Pryce Trevor
147	Heather Hardy
148	Janette Keyser
149	Vernon Keyser
150	John and Yvonne Abernethy
151	Veronica Hill
152	Michael Hill
153	Emidio Restall
154	P Restall
155	James Grieshaber

Submission	Individual/Organisation
156	John Hart
157	Nancy Fitt
158	Agnes-Mary Hanna
159	Martin Wheeler
160	Loretta Wheeler
161	Andrew Wheeler
162	Anne Walsh
163	Helina Farland
164	Confidential
165	Sally O'Grady
166	Leo McManus
167	J and EM Campbell
168	G and N Hagan
169	Margaret Hanna
170	Beverley Tearle
171	Confidential
172	Anna Vingerhoed
173	E and J Higgins
174	Mary Roth
175	Graeme Payne
176	Jacqueline Mackenzie
177	Judy Payne
178	M Moynahan
179	Dr Elizabeth Meagher
180	Diabetes Transplant Unit
181	JM Vink
182	Therese Winspear
183	Anne Archinal
184	JC Cridland
185	Margaret Ross
186	M Verschuer
187	Mary Dillon
188	Maureen Bellero
189	Betty Griffin
190	Margaret McNamara
191	Lynda O'Shea
192	B O'Hare
193	John Hogan
194	Margaret Bouffler
195	Jane Buttigieg
196	Pauline Hanrahan
197	Alvina D'Souza

Submission	Individual/Organisation
198	Lorraine Slater
199	S Sullivan
200	K Pigott
201	Grace Boncales
202	Crystal Rodricks
203	Lucy Skrinnikoff
204	Lourdes D'Souza
205	Margherita Griffin
206	Les D'Arcy
207	Dr Arthur Hartwig
208	BJ and CJ Robertson
209	Michael Rose
210	Marcia Smith
211	Kathleen Campbell
212	Christina Freese
213	Rita Bray
214	Dr Thomas Lynch OAM
215	Joan Cosgrove
216	Confidential
217	Professor Alan Mackay-Sim
218	The Fertility Society of Australia and Monash IVF
219	Kathryn Wojcicki
220	Joseph McDevich
221	Gwen Steffen
222	M O'Donnell
223	Mona McMahon
224	Josephine Ryan
225	Annette Rowley
226	Conny Drum
227	Patricia Frazer
228	Sharon Kohlhardt
229	M Grant
230	Marlene Wallace
231	Diana Clacy
232	Ann-Elise Cole
233	Danielle McKendry
234	Dr Nicholas Aroney
235	A.A Janssen
236	Manuel Carcellar
237	Chris Hilder
238	John Kurmann

Submission	Individual/Organisation
239	Louise Thompson
240	Hillas and Rhoda MacLean
241	Frank Burgess
242	R.J Perkins
243	Tony Flynn
244	Paul Groves
245	The Australian Society for Medical Research
246	National Civic Council
247	Allan Choveaux
248	Cootamundra Branch (NSW) of Catholic Women's League
249	Dunstan and Margaret Hartley
250	Barry and Ann Lock
251	Juli Bednall
252	Craig Scott
253	Helmut Bohn
254	Gerard Calilhanna
255	Owen Hitchings
256	Confidential
257	Dr Stephen Junk
258	Erica Brandalise
259	Australian Family Association(NSW)
260	Rodney Brydon
261	Ian Sinclair
262	Dr Harley Powell
263	Jeremy Peet
264	Denis Strangman
265	Jenny Chen
266	Confidential
267	Confidential
268	Judith Gerber
269	Marion Isham
270	Confidential
271	Richard and Carolyn Hawke
272	Bernadette Davies
273	Nola Drum
274	James Tayler
275	Jim Nicholls
276	Rosalie Ansell
277	Edward Roose

Submission	Individual/Organisation
278	Trisha Bosel
279	David Jenke
280	New Life Baptist Church in Dee Why Sydney
281	Denis Colbourn
282	Mark Emblen
283	Frank O'Sullivan
284	Kevin and Helen Harwood
285	Pauline O'Shea
286	Tony Quinn
287	Adam Johnston
288	Right to Life Australia
289	Pamela Cornish
290	Joanne Edmunds
291	Michael and Gillian Gonzalez
292	Darryl Shirt
293	June Johnston
294	Roger Armstrong
295	Basil Bryan
296	John Cooney
297	Marion Rogers
298	Philip Barnes
299	Luke Scott
300	Laurence Whitehead
301	Lance and Fiona Drum
302	Farther Afrian Head
303	Peter Crouch
304	Peter Downie
305	Debbie Halton
306	Confidential
307	Confidential
308	Spinal Cure Australia
309	Jane McEvoy
310	Dr Kevin Ward
311	Professor Malcolm Parker
312	Bio21 Australia Ltd
313	Greg Byrne
314	Matthew Lawler
315	Dr Gail Tulloch
316	Rick Maude
317	Tony King
318	Stem Cell Sciences Ltd

Submission	Individual/Organisation
319	Dr David Gawler
320	Jon Guyer
321	Professor Phil Waite
322	Peter Wright
323	Ian Kennedy
324	Leo Francis Donnelly
325	Brett Cunningham
326	Christine Hall
327	Ingrid Teda
328	Confidential
329	Matthew Beecroft
330	Confidential
331	Dr Colin Martin
332	Confidential
333	Confidential
334	Confidential
335	Confidential
336	Chantahl Rodwell
337	Confidential
338	Confidential
339	Sarah Marshall
340	Helvi Rossi
341	Sashi Sivagnanam
342	Confidential
343	Malcolm Lambert
344	Michelle Roberts
345	Confidential
346	Confidential
347	Dean Bosman
348	Julian Bosman
349	Simon Manchester
350	National Association of Catholic Families
351	Religious Freedom Institute Inc
352	Confidential
353	Professor Chris O'Neill & John McLaughlin
354	Family Life International (Aust) Ltd
355	Ganesh Sahathevan
356	John Byrnes
357	Rae Timmins
358	Glenys Darnell
359	John Kramer
360	Endeavour Forum Inc
361	Australian Family Association
362	L Durkin
363	Church By The Bay
364	The Queensland Institute of Medical Research
365	Mary Towler
366	Debora Shiosaki
367	Madeleine Edgar
368	Caroline Hampton
369	Kevin & Marie Sullivan
370	Joyce Flint
371	Alan Bolin
372	Dr John Broomhead
373	Christian Democratic Party (WA branch)
374	John McCormack
375	Lyn Kelly
376	Queensland Right to Life
377	Alex Everson
378	Noreen Everson
379	Farther Gerald Gleeson
380	Australian Family Association (ACT Branch)
381	Dr Joseph Santamaria
382	Alan Mitter
383	R Goulding
384	J Cartwright
385	Thalia Abela
386	Brian & Judy Magree
387	Fred & Mary Mauloni
388	Industrial & Social Research Associates Pty Ltd
389	Pauline Duggan
390	D Gould
391	Professor HW Gordon Baker
392	Caroline Chisholm Centre for Health Ethics Inc
393	MYO Australia
394	Movement Disorder Society of Australia

Submission	Individual/Organisation
395	Gerard Flood
396	Stem Cell Ethics Australia
397	Council of the St Thomas More Society
398	Chris Svolos
399	Shop Distributive & Allied Employees Association
400	Julie Cameron
401	Dr Andrew Fry
402	Confidential
403	Confidential
404	Bryan Pevely
405	Confidential
406	Christian Adult Social Institute Inc (CASI)
407	Country Women's Association of New South Wales
408	Donna Cooper and Nigel Stobbs
409	Confidential
410	Confidential
411	Confidential
412	Confidential
413	Dr Peter Williamson
414	Jacqueline Buchanan
415	Confidential
416	Arthur Donnelly
417	Confidential
418	Confidential
419	Queensland Bioethics Centre
420	Dr Bruce Wearne
421	Dr Brian Pollard
422	Confidential
423	James Guest
424	Confidential
425	Confidential
426	Dr Tamara Pollock
427	Confidential
428	Richard Cho
429	Confidential
430	Tania McLeod-Yu
431	Confidential
432	Armen Nalbandian
433	Julia Zahra
434	Dr David Swanton
435	Lesley Hicks
436	Andrew Lamb
437	Theresa de Gabriele
438	Confidential
439	Confidential
440	Dr Albert Reece
441	Justin Lees
442	Kenneth Glasgow
443	Confidential
444	Nick Overton
445	Confidential
446	Joel Wight
447	Mary Holland
448	Bradley Dunn
449	Third-year Bachelor of Biomedical Science Students, Univeristy of Melbourne
450	AusBiotech
451	Southern Cross Bioethics Institute
452	Joshua Ferrara
453	Confidential
454	Julie Smith
455	Dr Robert Eagleson
456	Rosemary Langford
457	Dr June Westwood
458	Taito Peura
459	Lesley Ramsay
460	Dr Kevin Wilkinson
461	Grant Wardell-Johnson
462	Erin Carter
463	Greenbank Susan
464	Rachel Jenner
465	Confidential
466	Ben Gooley
467	Confidential
468	Anthony Douglas
469	Margaret-Mary Althaus
470	Confidential
471	Ann Cunningham

Submission	Individual/Organisation
472	Michael Allen
473	Isobel Gawler
474	Professor Jonathan Morris
475	Dr Vivek & Annu Phakey
476	Ernest McDonald
477	Confidential
478	Kathryn Brennan
479	Confidential
480	Professor Patrick Quirk
481	Australian Catholic Bishops Conference
482	Confidential
483	Heather Halloran
484	Confidential
485	Nigel Fortescue
486	Uniting Church in Australia, Synod of Victoria and Dr Rosalie Hudson
487	David Walker
488	Anita Blandford
489	Shannon Payne
490	Michael Keith
491	Gordon Killow
492	Matthew Breeze
493	Susan Davy
494	Catholic Archdiocese of Sydney
495	Confidential
496	Timothy Mildenhall
497	John C Payne
498	Alex Zavadil
499	Lee Pevely
500	Confidential
501	Dr Daniel King
502	Dr Nicholas Tonti-Filippini
503	Baptist Churches of Tasmania
504	Brad Vale
505	Australian Christian Lobby
506	Diabetes Australia-NSW
507	Confidential
508	Victoria Walker
509	Dr Martin Pera and others
510	Matthew Heazlewood
511	Martin Shanahan
512	Elisa Zavadil
513	Stan Fishley
514	Confidential
515	Dr Rachel Ankeny, Associate Professor Susan Dodds, Associate Professor Wendy Rogers
516	Mr Benedict Smith and Ms Julianna Smith
517	David Mitchell
518	Assemblies of God in Australia
519	Confidential
520	Geoff Mulherin
521	Dr Jennifer Roberts
522	Helen Kyzintas
523	Anne-Maree Althaus
524	Confidential
525	Trudy Masters
526	Confidential
527	Confidential
528	Joe Daniel
529	Confidential
530	Craig Donnelly
531	Presbyterian Church of Victoria
532	Jason Poulos
533	Leanne Chronican
534	Heather J Payne
535	Australian Stem Cell Centre Ltd
536	Diabetes Australia-NSW
537	Government of Victoria
538	Dr Colin McQueen
539	Cynthia Zacest
540	Presbyterian Church of Australia in New South Wales
541	Ronald Butterworth
542	The Women's Christian Temperance Union of WA, Inc
543	Knights of the Southern Cross (Queensland) Inc
544	Lutherans For Life

Submission	Individual/Organisation
545	National Party of Australia – Victoria
546	Jane Munro
547	Lutheran Church of Australia
548	Farther Graham Castle
549	Pro-Life Victoria Inc
550	Plunkett Centre for Ethics
551	Roman Catholic Diocese of Parramatta
552	Professor T John Martin
553	Adam Koch
554	Elva Deme
555	Mario Andreallo
556	Michael Horgan
557	Charles Bagguley
558	Katherine Milesi
559	Kathleen Donohue
560	David & Jackie Gooding
561	Helen Ellery
562	Roma Wilson
563	David & Marie Oldfield
564	John Bohan
565	Margaret Ker
566	Simon Millie
567	Dr Ruth Nicholls
568	Peta York
569	Louise Fairhurst
570	Desmond & Josephine Kenneally
571	Margaret Powell
572	Norma Templeman
573	Catholic Womens League Australia Inc
574	Jane Robertson
575	Reverend D Clarnette
576	The South Australian Department of Health
577	Lance Wearmouth
578	Retina Australia
579	Dr Brian Coman
580	Pam Forno
581	Marie Langtree
582	Veronique Fomiatti

Submission	Individual/Organisation
583	Keith Black
584	Gary Smitham
585	Suzanne Martin
586	Margaret Hendy
587	Damer Walsh
588	Frances Tincknell
589	Pauline DeBrevi
590	Judith Bond
591	Frank & Anne Rasenberger
592	Kenneth & Patricia Moran
593	Paul Sheridan
594	Danny & Julie Russell
595	Frank Van Rees
596	Barney Tomasich
597	Clifford Headford
598	Confidential
599	Australian Federation of Right to Life Associations
600	Judith Northover
601	Professor Julian Savulescu
602	Iain Smith
603	Coalition For The Defence of Human Life
604	Augusto Zimmermann
605	Peter Kamsma
606	Polly Seidler
607	John Simpson
608	Michael Sobb
609	Dr Adam Cooper
610	Lynelle Lockrey
611	Ellis Murphy
612	Cheryl Clough
613	Confidential
614	Australian Association of Neurologists
615	Diane Garvey
616	Dr John and Evelyn Billings
617	K Grainger
618	Neil & Barbara Harvey
619	The Ovulation Method Research & Reference Centre of Australia

Submission	Individual/Organisation
620	Christian Reformed Churches of Australia — Classis WA
621	Sam Hatch
622	Andrea Beevers
623	Frans Zylstra
624	Salt Shakers
625	Dr Les & Verna Hemingway
626	Daphne McClelland
627	Mike McAuliffe
628	Confidential
629	Ruth Cummings
630	Dr Peter McCullagh
631	Peter & Marianne Murray
632	Catholic Women's League Australia, NSW Inc (Armidale Tamworth branch)
633	Jan Huggett
634	Anthony & Daphane Smith
635	Catholic Women's League of Victoria & Wagga Wagga Inc
636	Rob Nyhuis
637	Right to Life Australia
638	Toowoomba Diocesan Catholic Women's League
639	Bruno & Margaret D'Elia
640	The Australian Family Association (Victoria)
641	Paul & Leonie Johnson
642	Christian Democratic Party (Victoria) Inc
643	Susan Pollock
644	Craig Tenkate
645	Alan Hoysted
646	Confidential
647	Reverend Philip Wheeler
648	David Perrin
649	Marianne Bagguley
650	Darilyn Adams
651	Erhard Lorrain
652	Neil Herbert
653	Robert & June Mears
654	Geoff & Lesli Findlay
655	Patrick Healy

Submission	Individual/Organisation
656	Aaron Izzard
657	Do No Harm — Australians for Ethical Medical Research
658	Emily O'Connor
659	Merle Ross
660	Paula Vanoploo
661	Lois Fong
662	Confidential
663	Elizabeth Chung
664	Gabrielle Walsh
665	Luke Davis
666	Nola Kenner
667	Jennifer Whately
668	Joy, Antonia and Amy Gilbert
669	Sharlene and Russell Mellor
670	Gregory Smith
671	Ray Barbero
672	Denise Carroll
673	Reverend Stefan Slucki
674	James Crockett
675	Denise den- Bakker
676	Farther Frank Monahan
677	Ian & Jillian Coutts
678	Roslyn & Emma Lee
679	Lesa Meese
680	David Short
681	The Australian Federation of Disability Organisations (AFDO)
682	World Federation of Doctors who Respect Human Life (Victoria Division)
683	Yvonne Pratt
684	Peter Lowe
685	Dr Barry Groves
686	Catholic Women's League of Victoria & Wagga Wagga Inc
687	Confidential
688	Francis Simm
689	Judith Heffernan
690	Pauline Jenkins
691	J Mullaney
692	A Johnson

Submission	Individual/Organisation
693	Adrian Harris
694	Confidential
695	J Nash
696	Albert & Anne Schuoler
697	H Hansen
698	Suzy Pompor
699	Joseph Coleiro
700	Ral Italiano
701	P Brady
702	Grace Stuart
703	Ronald Ring
704	Catherine Kemp
705	Clare Johnston
706	Michelle Pedersen
707	Confidential
708	Edith Mott
709	Poonam Relan
710	Dr Vikas Bhasin
711	Margaret Keogh
712	Doreen Garniss
713	V Pompor
714	Eric La Bonne
715	Natalie La Bonne
716	Steve Blencowe
717	L Walsh
718	Charles Thornley
719	D & C Van Galen
720	Eileen Fitzpatrick
721	John Chenhall
722	Martin Geluk
723	Anna O'Brien
724	Dion and Cath Nohlmans
725	Bartle Kempster
726	Brett O'Neill
727	Paul O'Connor
728	Karis Anders
729	Shane Baxter
730	Valentino Adami
731	Reg & Denise Hazzard
732	Amy Quinn
733	Colin & Helen Hilder
734	Kevin Gould
735	Peter Phillips
736	Brendan Cusack
737	Ben O'Brien
738	J Lonergan
739	Brother Dominic Levac
740	Brother Jack Mardesic
741	John Gill
742	Barbara Edwards
743	Mary & Keith King
744	Leslie Woodhead
745	V Hickey
746	Kathleen Hampshire
747	Stephanie Burke
748	Jane Byrne
749	Irene Kelly
750	E & M Boyd
751	C McCue
752	Angela Goodwin
753	Robert Doran
754	Catherine Hilder
755	William & Sandra Tento
756	Imelda Aslett
757	Allan Lutvey
758	DC Hegerty
759	Winnie Chu
760	Matthew Grinter
761	Anna Deuar
762	Krzysztof Deuar
763	Norman James Schuler
764	Marie Prince
765	BT Miller
766	JH Jesse
767	Dr Doris Barnes
768	Fay O'Grady
769	John Killigrew
770	FP Haire
771	John Wright
772	James Pearce
773	David Forster
774	Peggy & Leo Bohan
775	Marshall McKelson
776	Mary Dowlings

Submission	Individual/Organisation
777	Margaret Healy
778	David Rea
779	Tom Clair
780	Anglican Church, Sydney Diocese
781	Dr Teija Peura
782	Government of Western Australia
783	David Smith
784	Michael Carey
785	Rita Joseph
786	Professor Paul Simmons
787	Women's Forum Australia
788	Margaret Rose Althaus
789	Confidential
790	National Health and Medical Research Council (NHMRC)
791	Sally Morrison
792	Patricia Buchiw
793	CA Barbetti
794	M Booker
795	Margaret & John Morgan
796	Catholic Archdiocese of Sydney
797	Thelma Brailey
798	R Bourne
799	Carmel Ford
800	Judith Eldridge
801	D Purcell
802	Esma Adams
803	Mary McInerney
804	Sharron Coleman
805	L & P Smyth
806	Margaret Brennan
807	Mary Price
808	John Young
809	Albert Malouf
810	Jill Van Dorsselaer
811	Nev Wells
812	Patricia Keeghan
813	Norm Auricht
814	Deirdre Lyra
815	Maria Scully
816	Anglican Church of Australia
817	Pamela Stamm
818	Catholic Parish of Inglewood, Bridgewater & Marong
819	Sydney IVF Ltd
820	Christian Democratic Party (New South Wales)
821	Margaret Chisholm
822	W & A Stephens
823	Gerard & Antoinette Keane
824	Jan Finlay
825	Robert Dsmak
826	Joan Apthorp
827	Professor Colin J Apelt
828	Kathleen Adams
829	Marijana Baric
830	Pat Mullens
831	Willie Chenhall
832	P & J Cronin
833	Confidential
834	Confidential
835	Mary Allen
836	FM & NF Hickey
837	Keith McKenna
838	Confidential
839	Lola & Josef Tarnawski
840	Jo Cook
841	Francis Underwood
842	R Osmak
843	Lorna Stokes
844	Richard Stokes
845	June Neilsen
846	David Duckett
847	Moya & Leo Morrissey
848	Ian Simmonds
849	M Doohan
850	LN Robinson
851	PA Thurbon
852	WJ Steeth
853	HJ Murphy
854	JJ Bartley
855	BW Foley

Submission	Individual/Organisation
856	JC Lloyd
857	GJ Fenning
858	FA Kenna
859	JJ Heanue
860	PF McAdam
861	WJ Johnson
862	AJ Mahoney
863	M Callaghan
864	K Baxter
865	James & Linda Bavas
866	Marjory Lewis
867	John Carter
868	JW Pacey
869	Matthew & Leonie White
870	Mary Harrold
871	Confidential
872	Robert Daley
873	Margaret Bellamy
874	S & L Recklies
875	FW Anderson
876	Thomas Lawless
877	Dennis Flentje
878	M & C McCaughan
879	Helen Casanova
880	C & J Donovan
881	Cecilia Lee
882	Margaret Dennis
883	Sister Josephine Carrol
884	Diana Fox
885	O & K Charles
886	G Osmak
887	James Hancock
888	Confidential
889	Rod Gruggen
890	Scientists in Reproductive Technology
891	Festival of Light Australia
892	Robyn Ellershaw
893	Dr Clement Persaud
894	Knights of the Southern Cross (Victoria)
895	Centre for Worldview Studies

Submission	Individual/Organisation
896	Reverend Brian Carey
897	Confidential
899	ACCESS (Australia's National Infertility Network Ltd)
900	Sandra Dill
901	Angela Hutchins
902	Sarah Dunlop
903	Katrina McClement
904	Chris Holmes
905	Joy McCook
906	Confidential
907	Kaia Smith
908	Nikki Milne
909	Joy Woodhead
910	B & G Peck
911	Confidential
912	Confidential
913	I & V Herft
914	Carmel Pit
915	L Maureen Oswald
916	J, C & B George
917	Clare Zavadil
918	Peta Secombe
919	Maureen Burges
920	J Franchi
921	George Charabie
922	Marion McLennon
923	Connie Mirabella
924	Agnes Catill
925	Brandon & Wendy Coleman
926	Kerrianne Springford
927	Dr Leslie Cannold
928	Cindy Ives
929	John & Sharee Voda
930	Queensland Government
931	Confidential
932	Dr Elizabeth Finkel
933	Confidential
934	Alice Hampson
935	Andrea Alexander
936	Confidential
937	Confidential

Submission	Individual/Organisation
938	Confidential
939	Confidential
940	Lyndell Williamson
941	Knights of the Southern Cross SA Inc
942	Denis & Helen Bowman et al
943	Confidential
944	Confidential
945	Confidential
946	Confidential
947	Confidential
948	Confidential
949	Confidential
950	Confidential
951	Rowena Verney
952	Confidential
953	Confidential
954	Physical Disability Council of Australia (PDCA)
955	Confidential
956	Confidential
957	Confidential
958	RSJ Simpson
959	CM Love
960	ZF Cruise
961	D, B, N & C Athayde
962	BA Tierney
963	Maureen Asmatage
964	T Lynch
965	A, P & L Christoforidis
966	K Kirwan
967	Helen Donkin
968	D Williams
969	Leo Mahoney
970	J Speirs
971	Joan Larsen
972	Leo Fitzsimon
973	John Casanova
974	Elizabeth Bambrick
975	The Hon John Murphy MP
976	Attorney-General's Department, Criminal Justice Division

Submission	Individual/Organisation
977	G Carusi
978	Kathleen Higgins et al
979	Veronica Pecchere
980	Margaret Blomfield
981	J Neldeia
982	Patrick Sibly
983	P Zimmermarn
984	Peter Dwyrdam
985	Coalition for the Defence of Human Life
986	Mary Chickerio
987	Thomas Bielenberg
988	J Vardelyt
989	Bruce & Helen Mitchell
990	H Catheson
991	Rosemary Manchester
992	Elizabeth Arvendell
993	Roslyn Deal
994	Corinne O'Loughlin
995	Anglican Diocese of Melbourne
996	Pat Stewart RAN Rtd
997	Richard and Beverley Grant
998	Moya Potts
999	Diana McIntosh
1000	N Where
1001	FM Hugh
1002	Sister Mary Tullos
1003	Francis Hemiekev
1004	Marion and Ralph Billing
1005	Miss Carryl Conkell
1006	Students at the ASCC and Monash Immunology and Stem Cell Laboratory
1007	Sophie Panopoulos MP
1008	Claire McManus
1009	Ross and Sue Fraser
1010	The Hon Ron Boswell
1011	S Murphy
1012	C Laffy
1013	G Laffy
1014	Senator John Hogg
1015	John Garlick

Submission	Individual/Organisation
1016	NSW Government
1017	Senator Grant Chapman
1018	David Bernard
1019	Minister for Education Science and Training
1020	SR Downs
1021	PJ McClear
1022	Mary Boskovic
1023	Alex Juricev
1024	Louise McManus
1025	Matthew Lee
1026	Redemptorist Community
1027	John Forrest
1028	Catholic Doctors Association of Victoria
1029	Jan Wilson
1030	Goolmangar Branch of the Mothers Union
1031	The Hon John Brumby
1032	Professor John Hearn
1033	The Hon Jackie Kelly MP
1034	VA Wigzell
1035	Confidential

Appendix 4 List of witnesses

Thursday 1 September 2005, Adelaide

Hearings

Dr Sheryl de Lacey, Research Centre for Reproductive Health, University of Adelaide

Professor Peter Rathjen, Executive Dean, Faculty of Sciences, University of Adelaide

Associate Professor Wendy Rogers, Department of Medical Education, Flinders University

South Australian Council on Reproductive Technology, represented by Dr Peter Woolcock, Deputy Chair

Southern Cross Bioethics Institute, represented by Dr Greg Pike, Director

Associate Professor Jeremy Thompson, Deputy Director, Research Centre for Reproductive Health, University of Adelaide

Private meetings

NHMRC Licensing Committee:

- Members
  - Professor Jock Findlay (Chair)
  - Professor Don Chalmers (Deputy Chair)
  - Professor Peter Illingworth
  - Dr Graham Kay
  - Dr Helen Szoke
  - Dr Julia Nicholls
  - Associate Professor Christopher Newell
  - Professor Bryan Campbell

South Australian Government officials:

- Ms Jean Murray, Principal Consultant, Ethico-Legal Reform, Department of Health
- Ms Helen van Eyk, Research Policy and Ethics Unit, Department of Health
- Ms Leanne Noack, Secretariat of the South Australian Council on Reproductive Technology

Monday 5 September 2005, Canberra

Private meetings

Australian Government:

- Minister for Ageing, the Hon Julie Bishop MP
- Minister for Industry, Tourism and Resources, the Hon Ian Macfarlane MP

Thursday 8 September – Friday 9 September 2005, Sydney

Hearings

ACCESS (Australia's National Infertility Network), represented by:

- Ms Sandra Dill, Executive Director
- Ms Debbie Jeffrey, Board Chair

Anglican Archdiocese of Sydney, represented by:

- Reverend Dr Andrew Cameron, Chair of the Social Sciences Executive
- Reverend Dr Andrew Ford, Assistant Minister, St Barnabas, Broadway

Dr Rachel Ankeny, University of Sydney

Catholic Archdiocese of Sydney, represented by the Most Reverend Professor Anthony Fisher, auxiliary bishop to the Most Reverend Dr George Pell, Archbishop

Dr Michael Carey, University of Technology Sydney

Coalition for the Advancement of Medical Research Australia, represented by Ms Joanna Knott, Director, Spinal Cure Australia

Juvenile Diabetes Research Foundation, represented by Mr James Shepherd, spokesperson

Motor Neurone Disease Association of New South Wales, represented by Dr Paul Brock, Chair

Professor John Rasko, Group head, Gene and Stem Cell Therapy, Centenary Institute of Cancer Medicine and Cell Biology

Professor Julian Savulescu, Director, Oxford Uehiro Centre for Practical Ethics, University of Oxford

Dr Kuldip Sidhu, Diabetes Transplant Unit, Prince of Wales Clinical School

Associate Professor Bernadette Tobin, Director, Plunkett Centre for Ethics, Australian Catholic University

Professor Alan Trounson, Director, Monash Immunology and Stem Cell Laboratories, Monash University

Private meetings

Mr Craig Cormick, Manager, Public Awareness, Biotechnology Australia

New South Wales Government officials:

- Professor Michael Reid, Director General of Health
- Ms Kerry Doyle, Executive Director, Ministry for Science and Medical Research
- Ms Suzanne Pierce, Principal Policy Officer, Ministry for Science and Medical Research
- Mr Ben Hewitt, Social Policy Branch, The Cabinet Office
- Ms Corena Sloper, Social Policy Branch, The Cabinet Office

Site visit

Sydney IVF:

- Professor Robert Jansen, Medical Director
- Reverend Dr Ivan Head, Chair of Sydney IVF Ethics Committee
- Ms Rebecca Hislop, Project Manager and Secretary to Ethics Committee
- Ms Sandra Dill, ACCESS (Australia's National Infertility Network) and member of Sydney IVF Ethics Committee
- Dr Teija Peura, biologist

Monday 19 September – Tuesday 20 September 2005, Brisbane

Sister Regis Mary Dunne, Mater Private Hospital

Professor Michael Good, Director, Queensland Institute of Medical Research

Professor Wayne Hall, Director, Office of Public Policy and Ethics, University of Queensland

Dr Keith Harrison, Scientific Director, Queensland Fertility Group

Associate Professor Melissa Little, Institute for Molecular Bioscience, University of Queensland

Associate Professor Malcolm Parker, Associate Professor of Medical Ethics, School of Medicine, University of Queensland

Professor Alan Mackay-Sim, Deputy Director, Eskitis Institute for Cell and Molecular Therapies, Griffith University

Professor Derek Morgan, Professor of Health Care Law and Jurisprudence, Cardiff Law School, Cardiff, Wales

Professor John Morgan, Director of the Australian Institute of Ethics and the Professions, St John's College, University of Queensland

Thursday 29 September – Friday 30 September 2005, Melbourne

Hearings

Professor Agnes Bankier, Director, Genetic Health Services Victoria

Australian Academy of Science

- Professor Bob Williamson
- Professor Suzanne Corey (Director, Walter and Eliza Hall Institute)

Dr Leslie Cannold, Centre for Applied Philosophy and Public Ethics, University of Melbourne

Caroline Chisholm Centre for Health Ethics, represented by:

- Reverend Dr Norman Ford, Director
- Mr Michael Herbert

Fertility Society of Australia, represented by Dr Adrianne Pope

Reverend Dr Colin Honey, Chair, Stem Cell Ethics Australia

Professor Paul Komesaroff, Director, Monash Centre for the Study of Ethics in Medicine and Society, Monash University

Dr John McBain, Director, Melbourne IVF

Emeritus Professor T Jack Martin, St Vincent's Institute of Medical Research, University of Melbourne

Reproductive Technology Accreditation Committee, represented by Professor Douglas Saunders

Right to Life, represented by:

- Ms Margaret Tighe, President
- Dr Mathew Piercey

Uniting Church, represented by

- Reverend Ross Carter
- Dr Rosalie Hudson

Victorian Government:

- The Hon John Brumby MLA, Victorian Treasurer and Minister for Innovation

Victorian Infertility Treatment Authority, represented by:

- Ms Louise Johnson, Chief Executive Officer
- Professor Jock Findlay, Chair

Professor Louis Waller, Monash Law, Monash University

Private meetings

Victorian Government:

- Premier of Victoria, the Hon Steve Bracks

AusBiotech, represented by:

- Professor Simon Carroll
- Dr Megan Munsie
- Ms Anita Hirschhorn

Site visit

Australian Stem Cell Centre (meetings with personnel from the Australian Stem Cell Centre, Monash Immunology and Stem Cell Laboratory, and Stem Cell Sciences Ltd):

- Australian Stem Cell Centre
  - Dr Hugh Niall (CEO)
  - Professor Stephen Livesey
  - Dr Dianna DeVore
  - Dr Andrew Elefanty
  - Ms Michelle Singhe
- Monash Immunology and Stem Cell Laboratory
  - Professor Ed Byrne (Dean of Medicine)
  - Professor Graham Jenkin
  - Dr Ed Stanley
  - Dr Andrea Lines
- Stem Cell Sciences Limited
  - Dr David Newton (General Manager)
  - Dr Megan Munsie (Development Manager)

Friday 7 October 2005, Hobart

(Via videoconference)

Baptist Churches of Tasmania, represented by Mr Eric Lockett, Chair, Public Questions Taskforce

Professor Simon Foote, Director, Menzies Research Institute

Dr Bill Watkins, Director, Tasmania IVF

Friday 21 October 2005, Perth

Hearings

Professor Alan Harvey

Dr Anne Jequier, PIVET Medical Centre

Dr Stephen Junk, Scientific Director, Hollywood Fertility Centre

LJ Goody Bioethics Centre, represented by Reverend Dr Joseph Parkinson, Director

National Civic Council, represented by Mr Richard Egan, State President

Western Australian Reproductive Technology Council, represented by:

- Ms Antonia Clissa, Executive Officer
- Professor Mark McKenna, Deputy Chair

Dr Peter Williamson

Private meeting

Western Australian Government officials:

- Dr Sandra Webb, Reproductive Technology Unit, Department of Health
- Ms Daphne Andersen, Legal Services Branch, Department of Health
- Ms Deborah Andrews, Legal Services Branch, Department of Health
- Mr Babu Simon, Research and Clinical Policy Unit, Department of Health

Monday 31 October 2005, Darwin

Hearings

Northern Land Council, represented by Mr Gareth Lewis, Acting Manager, Anthropology Branch

Aboriginal Medical Services Alliance Northern Territory (AMSANT), represented by:

- Mr John Paterson, Chair
- Ms Pat Anderson, Executive Officer

Private meeting

Northern Territory Government officials:

- Dr Tarun Weeramanthri, Assistant Secretary, Strategy and Quality Division, Principal Medical Adviser and Chief Health Officer of the Northern Territory
- Ms Rachael Shanahan, Project officer, Department of the Northern Territory Chief Minister

Appendix 5 Discussion forums

The Legislation Review Committee (the Committee) organised three facilitated discussion forums:

8 September 2005; 4.30–6.30 pm, Intercontinental Hotel, Sydney

19 September 2005; 4.30–6.30 pm, Carlton Crest Hotel, Brisbane

29 September 2005; 4.30–6.30 pm, Sofitel Hotel, Melbourne

The purpose of the forums was to promote community and stakeholder discussion about the legislation reviews, identify key issues of community and stakeholder concern and explore options for the resolution of those concerns. Summaries of the discussions are available on the Legislation Review website: http://www.lockhartreview.com.au

Program

4.30	Opening and welcome from the Chair of the Legislation Review Committee
4.40	Introduction to legislation and issues
4.50	Discussion session 1: Scope and operation of the *Research Involving Human Embryos Act 2002*
5.20	Identification of other issues
5.30	Discussion session 2: Scope and operation of the *Prohibition of Human Cloning Act 2002*
6.00	Discussion session 3: Other issues (including import and export of embryos and stem cells)
6.15	Concluding comments and discussion
6.30	Close

Attendees

Legislation Review Committee

Members from:

The Hon John S Lockhart AO QC (Chair)

Professor Peter Schofield (New South Wales)

Associate Professor Ian Kerridge (New South Wales)

Professor Loane Skene (Victoria)

Professor Barry Marshall (Western Australia)

Associate Professor Pamela McCombe (Queensland)

Facilitator: Ms Sandra Gadd (Sydney and Brisbane forums); Mr Rob Diamond (Melbourne forum)
Technical assistant/writer: Dr Janet Salisbury, Biotext
Secretariat: Mr Rob Diamond, Dr Andina Faragher, Secretariat Australia
Observer: Mr Nicholas Duell, National Health and Medical Research Council

Participants

Sydney

Dr Rachel Ankeny	University of Sydney
Mr Craig Cormick	Biotechnology Australia
Mr George Jobling	Parkinson's (New South Wales) Inc
Associate Professor Susan Dodds	University of Wollongong
Reverend Dean Drayton	Uniting Church in Australia
Reverend Dr Andrew Cameron	Anglican Arch Diocese of Sydney
Reverend Dr Andrew Ford	Anglican Arch Diocese of Sydney
Dr Isabel Karpin	University of Sydney Law School
Ms Tamra Lysaght	University of Sydney
Dr Fiona Mackenzie	Unit for History and Philosophy of Science, University of Sydney
Ms Angie Middlehurst	Diabetes Australia (New South Wales)
Associate Professor Chris O'Neill	Human Reproduction Unit, Royal North Shore Hospital
Associate Professor Bernadette Tobin	Plunkett Centre for Ethics, Australian Catholic University
Professor Phil Waite	Neural Injury Research Unit, University of New South Wales

Brisbane

Ms Anne-Maree Althaus	Member of public
Dr Ray Campbell	Queensland Bioethics Centre and Catholic Archdiocese of Brisbane
Dr Peter Dodd	Biochemistry Department, University of Queensland
Sister Regis Mary Dunne	Mater Private Hospital, Mater Research Institute
Dr Astrid Gesche	Centre for the Study of Ethics, Queensland University of Technology
Mr Paul Groves	Member of public
Professor Alan Mackay-Sim	School of Biomolecular and Biomedical Science, Griffith University
Ms Mary Rofe	Member of public
Dr Gail Tulloch	Key Centre for Ethics, Law, Justice and Governance, Griffith University

Melbourne

Mr Bennett Foddy	Student, University of Melbourne
Mr Lincon Stamp	Student, Monash University
Dr Megan Munsie	Stem Cell Sciences Pty Ltd
Ms Anita Hirchhorn	AusBiotech
Ms Carrie Beetham	Person with Friedrich's ataxia
Ms Varilli Beetham	Carer
Ms Tamara Curran	person with Friedrich's ataxia
Mr Sean Lusk	person with cystic fibrosis
Ms Margaret Tighe	Right to Life Australia
Dr Mathew Piercy	Right to Life Australia
Dr Phillamina Tenni	GP/obstetrician, World Federation of Doctors Who Respect Human Life
Ms Babette Francis	Endeavour Forum Inc
Ms Madge Fahy	Catholic Women's League, Victoria
Mr Gary Allsop	person with a spinal cord injury, representing Spinal Cure Australia
Mr Fred Allsop	Carer
The Hon James Guest	Former Victorian parliamentarian
Mr Gerard Flood	National Civic Council
Dr Joe Santamaria	National President, Australian Family Association
Mr David Palmer	Convenor, Presbyterian Church of Victoria
Mr Michael Casanova	Victorian President, Australian Family Association
Reverend Ross Carter	Uniting Church
Reverend Dr Norman Ford	Caroline Chisholm Centre for Health Ethics Inc
Dr Rosalie Hudson	Uniting Church
Mr Lucien McMahon	Student, University of Melbourne
Professor Gordon Baker	Melbourne University
Reverend Allan Nichols	Anglican Church
Professor T Jack Martin	St Vincent's Institute of Medical Research

Dr Kerri Allen	Research Officer, Australian Family Association
Dr Elizabeth Finkel	Science author
Mr Joe de Bruin	Shop, Distributive and Allied Employees Association
Ms Lexi Neame	Research Officer, Infertility Treatment Authority
Ms Shannon Payne	Member of the public
Dr Richard Boyd	Monash University
Mr Andrew Fry	Member of the public
Mr Michael Herbert	Research Officer, Caroline Chisholm Centre for Health Ethics Inc
Ms Renee Kyle	Student, University of Wollongong

Appendix 6 Media release

Below is the text of advertisements placed in State and Territory dailies on 9 July 2005. The inquiry was advertised in the following papers: *Sydney Daily Telegraph*; *Melbourne Herald Sun*; *Adelaide Advertiser*; *West Australian*; *Northern Territory News*; *Brisbane Courier-Mail*; *The Canberra Times*; *Sydney Morning Herald*; *The Age*; *Hobart Mercury*; *The Australian*.

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

Call for written submissions

The Australian Government Minister for Ageing, the Hon Julie Bishop MP, has appointed the Legislation Review Committee to conduct independent reviews of Australia's Prohibition of Human Cloning Act 2002 and the Research Involving Human Embryos Act 2002. Together, the Acts establish a regulatory framework to prohibit certain unacceptable practices including human cloning and to regulate, through the National Health and Medical Research Council, research involving excess human embryos created through assisted reproductive technology.

The Committee is chaired by retired Federal Court judge, Justice John Lockhart AO QC. Reports of the Committee will be forwarded to the Council of Australian Governments and tabled in both Houses of the Australian Parliament by 19 December 2005. The Committee is required to consult with the Australian, State and Territory governments and a broad range of people with expertise or experience in relevant disciplines.

The Committee is calling for written submissions on the scope and operation of the two Acts. The Terms of Reference require it to take into account such matters as: developments in technology in relation to assisted reproductive technology; developments in medical research and scientific research and the potential therapeutic applications of such research; community standards; the applicability of establishing a National Stem Cell Bank; and a range of other matters.

The full Terms of Reference for the reviews and the links to the two Acts and Guidelines for Making a Submission are available at www.lockhartreview.com.au

The Committee is preparing an Issues Paper. This document will be available on the above website shortly. Interested parties who wish to make a submission should first register their interest at www.lockhartreview.com.au by logging their details and reading the guidelines for making a submission. Registered parties will be sent the Issues Paper as soon as it is released.

If you do not have access to the internet and wish to make an inquiry or a submission, please contact the secretariat as indicated below.

Public access to all documentation relating to the call for written submissions is available at www.lockhartreview.com.au or from the secretariat as indicated below.

The period for submissions to be lodged will close on 9 September 2005.

Further Information about the reviews can be obtained from:
Legislation Review Secretariat
Phone: (02) 6295-8481
Email: lockhartreview@secretariat.com.au

Glossary

Terms marked in **bold** are defined elsewhere in the Glossary.

Adult stem cell (non-embryonic 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 **embryo**s for the purposes of reproduction.
Blastocoel	The cavity in the **blastocyst** of the developing **embryo**.
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 fluid-filled 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.
Blastula	An early stage of embryonic development in primitive animals (including amphibia), equivalent to the **blastocyst** in mammals.
Bone marrow stromal cell	A **stem cell** found in bone marrow that generates bone, cartilage, fat and fibrous connective tissue.
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
Cell-based therapy	Treatment in which cells cultured in the laboratory are transplanted into a person to repair damaged or deficient cell populations or tissues. For example, nerve cells may be transplanted to repair damage to the nervous system, such as spinal cord injury.
Chimera	An organism containing two or more genetically distinct cell or tissue types. A chimeric **embryo** can be formed by inserting a cell (or cells) from one embryo into the early cell mass of another embryo.
Chromatin	Areas or structures within a nucleus of a cell, composed of **DNA** and proteins.
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. In terms of animals or humans, cloned individuals have the same genetic composition, or **genome**, as each other (compared with most individuals who have a unique genome composed of a mixture of their maternal and paternal genomes). Identical twins are clones of each other.
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.
Cytoplasm	The contents of a cell (apart from the **nucleus**) formed from a complex protein matrix, in which the cell's contents are suspended.
Cytoplasmic transfer	Injecting **cytoplasm** from the egg of a healthy woman into the egg of another woman to assist conception or to correct defects.
Cord blood cells	**Hematopoietic ('adult') stem cells** found in blood from the umbilical cord.
Differentiation	The process whereby an unspecialised cell acquires the features of a specialised cell, such as a heart, liver, or muscle cell.
Diploid	A full set of genetic material consisting of paired **chromosome**s, with one chromosome from each parental set. Most animal cells, except the **gametes**, have a diploid set of chromosomes. The diploid human **genome** has 46 chromosomes. *See also* Haploid, Somatic cell
Directed differentiation	Manipulating **stem cell** culture conditions to induce a cell to **differentiate** into a particular cell type.
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.
Ectoderm	Upper, outermost layer of a group of cells derived from the **inner cell mass** of the **blastocyst**. The ectoderm gives rise to skin, nerves and brain.
Embryo	The early developmental stage of an animal. *See* Human embryo
Embryoid bodies	Clumps of cellular structures that form when **embryonic stem cells** are cultured.
Embryonic germ cell	A cell found in a specific part of the **embryo** or **fetus**, called the gonadal ridge. These cells are the precursors of **gametes**.

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.
Endoderm	Lower layer of a group of cells derived from the **inner cell mass** of the **blastocyst**. The endoderm gives rise to lungs and digestive organs.
Extra-embryonic tissues	The tissues that are not part of the developing organism itself (the placenta, membranes, umbilical cord etc).
Feeder layer	A layer of cells (often irradiated animal cells) on which cells of interest may be grown in the laboratory.
Fertilisation	The process whereby male and female **gametes** unite.
Fetus	A developing human from two months after conception to birth.
Gastrula	Follows the **blastocyst** stage. The purpose of gastrulation is to position the three embryonic germ layers, the **endoderm**, **ectoderm** and **mesoderm**. During gastrulation, embryonic cells migrate through an opening within the **embryo** known as a **blastocoel**.
Gamete	A human sperm or egg cell (which is also known as an **oocyte**).
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.
Haploid	A single set of **chromosome**s (half the full set of genetic material) present in the egg and sperm cells of animals and in the egg and pollen cells of plants. Humans have 23 chromosomes in their reproductive cells. *See also* Diploid
Hematopoietic stem cell	A **stem cell** from which all the cells of blood develop.
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. (Definition from the *Research Involving Human Embryos Act 2002*)
Human embryo clone	A human **embryo** that is a genetic copy of another living or dead human, and was not created by the **fertilisation** of a human egg by a human sperm. (Definition from the *Prohibition of Human Cloning Act 2002*)
Hybrid	Offspring resulting from breeding between parents of two different species.
Implantation	The process when the **blastocyst** embeds into the endometrium (lining of the uterus) to form a pregnancy.

Imprinting	The ‘memory’ held by a **chromosome** about which parent it was inherited from. The memory is chemically ‘stamped’ into the **DNA** and can result in chromosomes behaving differently, depending on the parent of origin.
Intracytoplasmic sperm injection (ICSI)	An **assisted reproductive technology** technique where a sperm is injected into an egg to assist **fertilisation**.
In vitro	Literally ‘in glass’; in a laboratory dish or test tube; an artificial environment.
In vitro fertilisation (IVF)	An **assisted reproductive technology** technique in which **fertilisation** is carried out in the laboratory.
In vitro maturation of oocytes	A laboratory process whereby an immature oocyte (egg) is allowed to mature until it is capable of being fertilised by a sperm cell.
Inner cell mass	The cluster of cells inside the **blastocyst**. These cells give rise to the **primitive streak** and the developing embryo-proper and **fetus**.
Mesenchymal stem cells	**Adult stem cells** with the ability to generate cartilage, bone, muscle, tendon, ligament and fat.
Mesoderm	Middle layer of a group of cells derived from the **inner cell mass** of the **blastocyst**. The mesoderm gives rise to bone, muscle, and connective tissue.
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
Morula	A stage of embryonic development in animals, including the 16-cell phase, the 32-cell phase, and the 64-cell phase. The morula is produced by embryonic cleavage (the rapid **cell division** of the **zygote** with virtually no growth). The morula is a solid ball, but after this stage, the **embryo** hollows out to form the **blastocyst**.
Multipotent	Ability of a single **stem cell** to generate several different cell types of the body. For example, some bone marrow stem cells give rise to all types of cells in the blood but not other types of cells.
Neural stem cell	A **stem cell** capable of forming all types of nervous tissues as well as haematopoietic (blood-forming) elements.
Nuclear transfer	Term that includes **somatic cell nuclear transfer** and some other related methods, including transfer of a cell **nucleus** from cells other than **somatic cells** (such as from **embryonic stem cells**).
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. *See also* Parthenogenesis

Parthenogenesis	The development of an organism from an unfertilised egg cell. This process is relatively common in plants, but less so among animals. Some species of insects can produce large numbers of individuals by this process. Since a female parent is, in essence, **cloning** herself, parthenogenesis always produces female offspring.
Parthenote	An **embryo** resulting from **parthenogenesis**.
Patient-matched cell	Cells that are derived from a person's own cells (either by culture of adult cells or generation of **embryonic stem cells** by **somatic cell nuclear transfer**).
Preimplantation embryo	A fertilised egg that has not yet implanted into the uterus.
Preimplantation genetic diagnosis (PGD)	A procedure used to test **embryos** for genetic abnormalities before placing them into a woman to establish a pregnancy.
Plasticity	The ability of **stem cells** from one adult tissue to generate the **differentiate**d cell types of another tissue.
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 (**endoderm, mesoderm** and **ectoderm**).
Preclinical studies	Laboratory studies to investigate mechanisms of action and studies to show 'proof of principle' (efficacy) and safety in animal models (such as mice or rats).
Primitive streak	Thickening in the surface of an **embryo** that occurs at the **gastrula**tion stage and is the first clearly recognisable sign of the developing organism itself (that is, distinct from the placenta and other **extra-embryonic tissues**).
Progenitor cell (or 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.
Proliferation	Expansion of a population of cells by the continuous division of single cells into two identical daughter cells, and so on.
Pronuclei	The **haploid nucleus** of a sperm or egg before they fuse during **fertilisation.**
Regenerative or reparative medicine	Treatments in which cells are transplanted into specific sites in the body to repair damaged or deficient cell populations or tissues. *See also* Cellular therapy
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	Any cell from an animal at any stage of development except for **gametes** (eggs or sperm) or their precursors. Somatic cells have the **diploid** number of **chromosomes**.

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**. *See also* Adult stem cells, Embryonic stem cells, Totipotent, Pluripotent, Multipotent
Stromal cells	Nonblood cells derived from blood-forming tissues, such as bone marrow or fetal liver, which are capable of supporting growth of blood cells **in vitro**. Stromal cells that make this matrix within the bone marrow are derived from **mesenchymal stem cells**.
Subculturing	The process of growing and replacing cells in tissue culture for several days.
Surface markers	Surface proteins unique to certain cell types, which can be visualised using antibodies or other detection methods.
Syngamy	The stage of **fertilisation** when the **chromosomes** from the male and female **pronuclei** combine into a single **diploid** set.
Teratoma	A tumour composed of a disorganised mixture of cell types (including cells from all three embryonic germ layers). Teratomas are usually found in the ovaries or testes. They can be produced experimentally by injecting animals with **pluripotent stem cells** (this is used as a test to show that the stem cells have the ability to form various types of tissues).
Therapeutic cloning	Term previously used to describe **cloning** to generate **embryonic stem cells**.
Totipotent	A cell that has the capacity to give rise to all tissue types, including placental and other **extra-embryonic tissues**.
Transdifferentiation	The observation that **stem cells** from one tissue may be able to **differentiate** into cells of another tissue.
Trophoblast	The outer layer of cells of a **blastocyst.** The **extra-embryonic tissue** responsible for **implantation**, developing into the placenta, and controlling the exchange of oxygen and metabolites between mother and **embryo**.
Type 1 diabetes	Type of diabetes also known as insulin-dependent diabetes, which occurs mainly in childhood or early adolescence and lasts throughout life. It requires daily insulin injections for survival. The most common form is caused by the destruction of beta cells in the pancreas by the auto-immune system, leaving the pancreas unable to produce insulin.
Unipotent stem cell	**Stem cells** that only give rise to one cell type.
Viable material	Living cells capable of dividing and growing.
Zygote	A cell that is the result of **fertilisation**. That is, two **haploid** cells — usually (but not always) a sperm cell from a male and an egg cell from a female — merge into a single **diploid** cell called the zygote (or zygocyte).

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